EXHIBIT D

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: '318 PATENT INFRINGEMENT LITIGATION	)	C.A. No. 05-356-KAJ (consolidated)

OPENING EXPERT REPORT OF DR. JOSEPH T. COYLE

I. ACADEMIC AND PROFESSIONAL QUALIFICATIONS

1. Currently, I am the Eben S. Draper Professor of Psychiatry and Neuroscience at Harvard Medical School. For 10 years, I served as Chair of the Consolidated Department of Psychiatry at Harvard.

2. My expertise is in the area of neuropsychopharmacology, which is concerned with the biological basis for disorders of the brain and their pharmacologic treatment. My research focused on Alzheimer's Disease throughout the 1980's and early 1990's. In the late 1980's I performed original research concerning the impact of galantamine, a cholinesterase inhibitor, on the working memory of mice with lesions in the nucleus basalis of Meynert that partially mimicked the effects of Alzheimer's Disease. Later, I was involved in clinical studies concerning the impact of galantamine on the cognitive function and activities of daily living of patients living with Alzheimer's Disease.

A. Educational and Professional Background

3. I received my A.B. from the College of the Holy Cross in 1965 and my M.D. degree from The Johns Hopkins University School of Medicine in 1969. I completed an internship in pediatrics and a residency in psychiatry, both at Johns Hopkins. I also completed

two research fellowships, one at the National Institute of Mental Health, and one in neurobiology at the Marine Biological Laboratory.

4. I am licensed to practice medicine in Massachusetts and Maryland (inactive). I am also a certified member of the National Board of Medical Examiners and am board certified in Psychiatry by the American Board of Psychiatry and Neurology.

5. I have been associated with Harvard Medical School since 1991, and since that time I have been in my current position as Professor of Psychiatry and Neuroscience. From 1991 to 2001, I served as the Chair of the Consolidated Department of Psychiatry, which included the nine hospital programs of psychiatry affiliated with Harvard Medical School. Before coming to Harvard in 1991, I held several positions at The Johns Hopkins University School of Medicine, including Assistant Professor of Pharmacology from 1974 to 1976; Assistant Professor of Pharmacology and Psychiatry from 1976 to 1978; Associate Professor of Pharmacology and Psychiatry from 1978 to 1980; Professor of Neuroscience, Psychiatry and Pharmacology from 1980 to 1991; Director of the Division of Child Psychiatry from 1982 to 1991; and Distinguished Service Professor of Child Psychiatry from 1985 to 1991.

6. Throughout my career, I have served on the editorial boards of a variety of academic journals and served on a number of advisory boards. In particular, I have served as Editor-in-Chief of the Harvard Review of Psychiatry and the Archives of General Psychiatry. I have also served on the editorial boards of the Journal of Developmental and Behavioral Pediatrics, Developmental Brain Research, Neuropharmacology, the European Journal of Pharmacology, and the Journal of Neuroscience. I have had editorial responsibilities in connection with other journals, including Molecular Psychiatry, Molecular and Chemical Neuropathology, Synapse, Archives of General Psychiatry, the Journal of Neuroscience

Research, Neuropsychopharmacology, Neurobiology of Disease, Cerebral Cortex, Neuroscience, the Journal of Psychiatric Research, and the Journal of the American Medical Association, among others.

7. I have also consulted for a number of pharmaceutical companies on the development of Central Nervous System (CNS) drugs, including: Abbott Laboratories, Bristol Myers Squibb, Cephalon, Janssen, and Prestwick. I was also a consultant for Dr. Bonnie Davis (through her company Synaptech) in connection with galantamine and its analogs.

8. I have authored 7 textbooks, 363 articles, and 154 reviews and chapters. I have also supervised the theses of 14 doctoral candidates and have supervised the work of 25 post-doctoral fellows.

9. I have also been a member or fellow of and served in leadership positions in a number of professional organizations. In particular, I have held leadership roles in the Society of Neuroscience since 1980, and the American College of Neuropsychopharmacology since 1989. I am also involved with the American Society of Neurochemistry, the American Psychiatric Association, and the Alzheimer's Disease and Related Disorders Association.

10. My *curriculum vitae*, which describes the above information in greater detail, is attached as Exhibit A.

B. Prior Testimony

11. I have not testified in connection with any matter, other than this one, in the last four years.

C. Compensation

12. For my work in connection with this matter, I am being compensated at my usual rate of $350 per hour. My compensation is not linked in any way to the outcome of this litigation.

II. SCOPE AND REVIEW

13. I was asked to review the assertions of invalidity raised by the defendants in this case and to provide an opinion as to validity of the '318 patent in my capacity as an expert in neuropharmacology.

14. I was informed about objective considerations of non-obviousness and was asked to provide in this report my opinion about whether certain objective considerations of non-obviousness – specifically, unexpected benefits of galantamine and skepticism of others skilled in the art – support the validity of the '318 patent.

15. In reviewing the defendants' assertions and forming the opinions stated in my report, I relied upon my experience, my knowledge of the relevant literature and state of the art, and also reviewed the materials set forth in Exhibit B.

III. BACKGROUND

A. The '318 Patent

16. I understand that the application for the '318 Patent was filed in the U.S. Patent and Trademark Office on January 15, 1986, and I have been asked to comment on the state of the art as of that date.

17. In terms of the patent claims, I understand that only two claims of the '318 patent are at issue in this litigation, claims 1 and 4, and that the defendants have stipulated to the infringement those two claims.

18. Claim 1 of the patent claims: "A method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof."

19. Claim 4 of the patent claims: "A method according to claim 1, wherein said administration is oral and is in the range 10-2000 mg per day."

20. As a general matter, I understand the claims of the '318 patent to be directed to the treatment of Alzheimer's Disease, whether pre-senile or Senile Dementia of the Alzheimer's Type, using therapeutic doses of galantamine or its pharmacologically acceptable salts, including galantamine hydrobromide. By treatment, I include alleviation of the symptoms of Alzheimer's Disease, particularly the cognitive loss that is the central feature of the disease.

B. Alzheimer's Disease

21. Alzheimer's Disease is a progressive, degenerative disease of the brain that destroys memory, the ability to learn, reason, make judgments, communicate, and engage in activities of daily living. As the disease progresses, it is also characterized by neuropsychiatric symptoms, i.e., changes in personality and behavior, including apathy, anxiety, and hallucinations.

22. The ultimate cause of the disease remains obscure. However, it is characterized by two particular pathologic features: "plaques" and "tangles." The consequence of these plaques and tangles is disruption of neurotransmitter systems in the brain, compromised cell function, and ultimately cell death.

23. Alzheimer's Disease is associated with a range of neurotransmitter deficiencies, including norepinephrine, serotonin, somatostatin, vasopressin, and ß-endorphin. The impact on the cholinergic system is a decrease in activity in choline acetyltransferase, the enzyme that synthesizes the neurotransmitter acetylcholine, in patients with Alzheimer's Disease. Acetylcholine is crucial in the formation and retention of memory.

C. Secondary Considerations of Non-Obviousness

24. I understand that the validity of a patent can be established by objective or "secondary" considerations of the non-obviousness of the invention.

25. I also understand that one of these secondary considerations is the unexpected benefits of the drug – benefits of the invention that were not expected or known at the time the patent was filed, or in this case, January 15, 1986, by those skilled in the relevant art.

26. Another of these secondary considerations is skepticism expressed by those skilled in the art concerning the usefulness of the patented invention.

27. I have undertaken an analysis therefore of the results and benefits of the use of galantamine in the treatment of Alzheimer's Disease that were not expected or known to those skilled in the art as of January 15, 1986.

28. I have also performed a survey of the skepticism expressed by those skilled in the art concerning the usefulness of galantamine as a treatment for Alzheimer's Disease.

IV. SKEPTICISM OF THOSE SKILLED IN THE ART

A. Historical Understanding of Alzheimer's Disease

29. It was not until late 1960s that "senility" in the elderly was recognized as the result of a disorder – Senile Dementia of the Alzheimer's Type (SDAT) – that shared the same pathological stigmata (senile plaques and neurofibrillary tangles) of a rare disorder known as presenile dementia of the Alzheimer's type.

30. Through the 1970s, it became increasingly apparent that this disorder was a main cause of dementia and death in the elderly population of the country, including perhaps 50% of those over 85.

31. At that time, many were pessimistic that this disorder would respond to any pharmacologic treatment because of the widespread pathology in the neo-cortex in the brain. Some experts even called Alzheimer's Disease "brain failure," analogous to heart failure following severe cardiac damage.

32. In the mid 1970s, there were reports that choline acetyltransferase (CAT) – the neurochemical marker for cholinergic neurons – was reduced and that this reduction might be selective in Alzheimer's patients. CAT is the enzyme that is made in the cell body of pre-synaptic cholinergic neurons and is transported along the axon to the nerve terminal, where it functions to produce acetylcholine.

33. The organization of the cholinergic neurons and their function in the cerebral cortex was poorly understood at the time. My laboratory demonstrated that the cell bodies of the cholinergic neurons innervating the cerebral cortex resided in a region of the brainstem called the nucleus basalis of Meynert. Lesion of this region in rats and mice caused a selective reduction of cholinergic markers in the cortex similar to what was reported in Alzheimer's Disease. Subsequent studies showed that this lesion impaired recent or working memory, which is analogous to the cognitive impairments that are observed in early Alzheimer's Disease. However, it was also recognized that this lesion did not create in the rodent brain the senile plaques and neurofibrillary tangles thought to be central to Alzheimer's Disease.

34. Furthermore, these cognitive impairments in experimental animals could be reversed through enhancement of cholinergic function. These observations led to formulation of a hypothesis – the "cholinergic deficit hypothesis" – by a few neuropharmacologists in the early 1980s. This hypothesis posited that selective degeneration of cholinergic neurons in the basal forebrain (that is, the nucleus basalis of Meynert) and the resulting cholinergic deficits

might account for the cognitive impairments observed in Alzheimer's Disease and therefore might be a target for developing treatments for those cognitive impairments.

35. At the time, those neuropharmacologists were encouraged in this thinking by the then recent success of the use of l-dopa to correct the dopamine deficits associated with the selective degeneration of nigro-striatal dopaminergic neurons in Parkinson's disease. L-dopa is the chemical precursor for dopamine.

36. However, the "cholinergic deficit hypothesis" was progressively undermined by the demonstration that Alzheimer's Disease affected a number of important neurotransmitter systems, both innervating the cortex (like the noradrenergic neurons) or contained within the cortex (like somatostatin neurons).

37. Moreover, the failure of acetylcholine precursor therapy showed that the cognitive decline in Alzheimer's Disease was not susceptible to simple pharmacologic manipulation of the cholinergic system, unlike Parkinson's disease.

B. Skepticism Regarding Cholinergic Enhancement

38. In light of this background, there was considerable skepticism among neuropsychopharmacologists about the possibility of treating the cognitive decline in Alzheimer's Disease with a pharmacologic intervention to enhance cholinergic function. Clinicians, to the degree they were aware of this at all, were skeptical that the cognitive decline of Alzheimer's Disease was susceptible to pharmacologic treatment of any kind.

39. This skepticism was based on the facts that the lesions in the rodent brain did not replicate Alzheimer's Disease, that the disease affected many different neurotransmitter systems, and that acetylcholine precursor therapy failed, as described above.

40. As a result, many in the field elected to pursue an approach directed to brain metabolism or perfusion, such as the nootropic drugs. "Nootropic" means acting upon the

brain, and the nootropics were a class of compounds that were believed to affect brain functioning through unknown mechanisms. The leading nootropic was piracetam, a GABA relative, though a number of derivatives, including pramiracetam, aniracetam, and oxiracetam, were also tried. While the class appeared to facilitate learning and memory in animal studies, clinical trials failed to show cognitive improvement in Alzheimer's patients. Despite considerable research efforts, FDA has never approved a nootropic for treatment of Alzheimer's Disease.

C. Skepticism Regarding Cholinesterase Inhibitors

41. There was also, at the time, considerable skepticism of cholinesterase inhibitors as potential treatments for the cognitive decline in Alzheimer's Disease. This skepticism stemmed in part from the same factors that led to the skepticism regarding attempts to treat Alzheimer's Disease more generally through cholinergic enhancement, described above. However, there were also additional factors, specific to the class of cholinesterase inhibitors itself, that produced further skepticism concerning the potential for a cholinesterase inhibitor to serve as a treatment for Alzheimer's Disease.

42. First, there was the logical criticism that inhibiting cholinesterase degradation of acetylcholine released into the synapse would have little impact on overall cortical cholinergic neurotransmission, since the pathology of Alzheimer's Disease involves pronounced deterioration of pre-synaptic cholinergic neurons and hence substantial reduction of acetylcholine release at the synapse. In other words, the therapeutic effects of cholinesterase inhibition in treating Alzheimer's Disease depend upon the functioning of pre-synaptic cholinergic neurons, and leading to the concern that the degradation of pre-synaptic cholinergic neurons in Alzheimer's patients is too great to allow acetylcholinesterase inhibition to affect acetylcholine levels in a meaningful way.

43. This concern led to a preference for a direct agonist approach, or an approach using agents that bind to and activate receptors in the brain – as opposed to an approach that inhibits further degradation of acetylcholine. For example, Raymond Bartus, a highly regarded neuropsychopharmacologist whose responsibility at Lederle Laboratories was to find pharmacologic treatments, published a review (along with several coauthors) expressing skepticism of a cholinesterase approach and advocating muscarinic agonists as the most promising avenue for cholinergic therapy. Bartus, R., *et al.*, "The Cholinergic Hypothesis: A Historical Overview, Current Perspective, and Future Directions," in *Memory Dysfunctions: An Integration of Animal and Human Research from Preclinical and Clinical Perspectives, Annals of the New York Academy of Sciences* 1985; 444: 332-58:

> Recent reports that degeneration of cholinergic forebrain nuclei may account for the loss of CAT activity in Alzheimer's patients provides additional impetus for studies with cholinergic agonists. That is, if one assumes this degeneration plays a major role in the cognitive symptoms of the disease, then the most effective means available to treat the deficit would be to compensate for the loss of cholinergic input to the cortex and hippocampus by stimulating the surviving postsynaptic cholinergic receptors. (page 342)

44. Similarly, in the mid to late 1980s, a number of the leading researchers in Alzheimer's Disease – including Dr. Pierre Tariot of the University of Rochester, Dr. Robert Cohen of the National Institute of Mental Health, and Dr. Paul Newhouse of the Walter Reed Army Institute of Research – collaborated on a study of arecoline, a muscarinic agonist. As they explained in a 1988 publication, their work was motivated by skepticism of the prospects for a cholinesterase approach and the "theoretical advantage of the use of direct cholinergic agonists":

> Studies of the intravenous and oral use of physostigmine, a short-acting cholinesterase inhibitor, have demonstrated only limited improvement of cognitive function and clinical condition of some patients with dementia of the Alzheimer type (DAT). There are conflicting results about the clinical and cognitive effects of a different cholinesterase inhibitor, tetrahydroaminoacridine. [¶]

> The use of postsynaptic cholinergic agonists is a strategy of particular interest in Alzheimer's disease in view of the apparent deterioration in presynaptic cholinergic receptors combined with stability of postsynaptic receptors. (Tariot, P. N., *et al.*, "Multiple-Dose Arecoline Infusions in Alzheimer's Disease," *Arch. Gen. Psychiatry* 1988; 45:901-05.)

45. Examples of muscarinic agonists that have been pursued as possible treatments for Alzheimer's Disease include arecoline and xanomeline, the latter taken through large-scale clinical trials by Eli Lilly. Despite over twenty years of efforts, no muscarinic agonist has yet succeeded as a treatment for Alzheimer's Disease.

46. Second, there was considerable concern regarding lack of specificity in the mechanism of action. Aside from the cholinergic neurons located in the basal forebrain that participate in memory and attention processes, cholinergic neurons are involved in a broad array of vital functions both in the brain and the periphery. For example, cholinergic neurons are involved with the parasympathetic neurons that regulate gastrointestinal and cardiac function, as well as the motor neurons that control movement of our voluntary muscles. These systems are therefore all affected by acetylcholinesterase inhibitors.

47. Indeed, these systems are the target of biological weapons and insecticides. Therefore, there was considerable concern that a general inhibition of acetylcholinesterase on a chronic basis would be accompanied by unacceptable side effects and perhaps even death. Dr. R.J. Wurtman, for example, a highly distinguished neuropharmacologist at MIT, warned in the mid-1980s that "a drug that inhibits acetylcholinesterases everywhere, as physostigmine apparently does, and thus enhanced cholinergic transmission everywhere, would have too many side effects to be used clinically." (Wurtman, R.J., "Activation of Neurotransmitters in the Brain: Strategies in the Treatment of AD/SDAT," in C.G. Gottfries, ed.,

Normal Aging, Alzheimer's Disease and Senile Dementia: Aspects on Etiology, Pathogenesis, Diagnosis and Treatment 275-80 (Editions de l'Universite de Bruxelles: 1985)).

48. Third, there was a concern that an acetylcholinesterase inhibitor would reduce the synaptic levels of choline selectively at the cholinergic nerve terminal, causing cholinergic neurons to cannibalize their membranes to synthesize acetylcholine. Thus, there was a fear that use of a cholinesterase inhibitor would actually exacerbate the vulnerability of cholinergic neurons in Alzheimer's Disease to degeneration (Wurtman, 1985)).

49. In the view of many, the clinical studies done as of January 1986 on acetylcholinesterase inhibitors reinforced this skepticism, because those studies showed at best marginal and inconsistent results (e.g., Tariot, *et al., and* Bartus, R.T., *et al.*, above). Bartus, *et al.*, for example, compared the testing to date on cholinesterase and agonist approaches and found in favor of an agonist approach: "When the direct agonist arecoline was tested in aged monkeys, not only was significant improvement obtained in a delayed recall task, but the dose response effects were also more consistent from monkey to monkey, as compared to physostigmine. Similar results have also been reported with Alzheimer's patients." (page 342)

V. UNEXPECTED BENEFITS OF GALANTAMINE

50. In the mid to late 1990s, it was discovered that galantamine has the additional effect on cholinergic neurotransmission, aside from inhibiting acetylcholinesterase, of being an allosteric modulator of nicotinic acetylcholine receptors.

51. Acetylcholine activates two types of receptors, the muscarinic receptors and the nicotinic receptors. The muscarinic receptors affect cellular metabolism through G-proteins. Activation of muscarinic receptors in the brain is associated with working memory; in the body, those receptors are also associated with heart rate, vasoconstriction, and gut motility, among other functions.

52. Nicotinic receptors in the cortex have also been associated with working memory. In contrast, however, nicotinic receptors in the brain are coupled to a cation channel, so that activation results in depolarization (i.e., excitation) of the post-synaptic neuron. In addition, activation of nicotinic receptors, through excitation of the neuron, enhances the release of other neurotransmitters, such as norepinephrine and glutamic acid. In the body, nicotinic receptors mediate the action of acetylcholine released by motor neurons in controlling voluntary muscle activity.

53. Acetylcholinesterase inhibition affects muscarinic and nicotinic receptors indirectly, by slowing the degradation of acetylcholine released at the synapse. The released acetylcholine activates either receptor.

54. An allosteric modulator is an agent that acts at a site distinct and separate from the site at which the endogeneous neurotransmitter binds to and activates the receptor. The effect of the allosteric modulator is to alter the response of the receptor to its endogeneous agonist without itself directly activating the receptor.

55. The pharmacologic advantage of an allosteric modulator is that it can increase the response of the receptor to its endogeneous neurotransmitter at lower concentrations of that neurotransmitter without activating the receptor when the neurotransmitter is absent. The consequence is to preserve the temporal nature of the synaptic firing while compensating for the reduced release of neurotransmitter from damaged or impaired nerve terminals.

56. In essence, an allosteric modulator combines many of the advantages of a cholinesterase inhibitor – namely, preservation of the phasic quality of synaptic firing (indeed, better than acetylcholinesterase inhibitor, because the allosteric modulator does not prolong the

duration of action of the released acetylcholine) – with those of an agonist – namely, compensation for reduction in the levels of endogeneous neurotransmitters.

57. In the mid 1990s, Edson Albuquerque and Alfred Maelicke demonstrated that galantamine was a positive allosteric modulator of nicotinic receptors. They further identified the site on the nicotinic receptor molecule at which the galantamine molecule binds and acts, and they showed that this activity was not shared with the other acetylcholinesterase inhibitors that are now approved – namely, tacrine, donepezil, and rivastigmine. These effects of galantamine were shown to occur at concentrations associated with therapeutic use of the drug that enhanced nicotinic receptor response by 40-50%.

58. Several laboratories have confirmed the role of galantamine as a positive allosteric modulator of nicotinic receptors under different experimental conditions, including in live animal testing, and this role of galantamine is now generally accepted in the scientific literature (e.g., Schrattenholz, A., *et al.*, "Agonist Responses of Neuronal Nicotinic Receptors Are Potentiated by a Novel Class of Allosterically Acting Ligands," *Molecular Pharmacology* 49:1-6 (1996); Maelicke A., *et al.*, "Allosterically Potentiating Ligands of Nicotinic Receptors as a Treatment Strategy for Alzheimer's Disease," *Behavioral Brain Research* 113:199-206 (2000); Woodruff-Pak, D.S., *et al.*, "Mecamylamine Interactions with Galantamine and Donepezil: Effects on Learning, Acetylcholinesterase, and Nicotinic Acetylcholine Receptors," *Neuroscience* 117:439-447 (2003)).

59. The clinical consequences of the dual mechanism of action remain unsettled. However, some reasonable inferences can be drawn from the existing information. Galantamine is a less potent inhibitor of acetylcholinesterase than the other approved acetylcholinesterase inhibitors (and does not inhibit butyrylcholinesterase to any meaningful

degree). In addition, recent studies have shown that the level of cholinesterase inhibition achieved by galantamine at therapeutic doses is substantially below the levels of inhibition achieved by therapeutic doses of the other approved cholinesterase inhibitors. A recent study by Geerts, *et al.*, for example, concluded that levels of acute brain cholinesterase inhibition by therapeutic doses of galantamine are three to four times less than the levels achieved by therapeutic doses of donepezil (Geerts, H., *et al.*, "Brain Levels and Acetylcholinesterase Inhibition With Galantamine and Donepezil in Rats, Mice, and Rabbits," in *Brain Research* 1033:186-193 (2005), at 191). This led the authors to conclude, reasonably, in my view, that "in order to account for the same observed behavioral effects, an additional mechanism of action [for galantamine] is needed to explain this equivalent behavior." The logical conclusion, in light of present evidence, is that galantamine's other mechanism of action – namely, its positive allosteric modulation of nicotinic receptors – is contributing to its clinical effect on cognition in Alzheimer's Disease.

60. Also supportive of the clinical significance of this second mechanism of action is a recent head-to-head trial of galantamine and donepezil that observed that galantamine had a greater effect on aspects of cognition related to stimulation of neuronal nicotinic receptors. As the authors observed, "[i]n both the MMSE and ADAS-Cog/11 item analyses, larger between-group differences were observed in items associated with attention and executive function than in other items. These observations support the hypothesis that the allosteric modulation of neuronal nicotinic receptors by galantamine effectively enhances attention and executive function." Wilcock, G., *et al.*, "A Long-Term Comparison of Galantamine and Donepezil in the Treatment of Alzheimer's Disease," *Drugs Aging* 20:777-789 (2003).

61. In addition to its effects on cognition, galantamine has been shown to reduce the emergence of some of the neuropsychiatric symptoms associated with Alzheimer's Disease, such as agitation and lethargy. This may reflect the pre-synaptic activation by nicotinic receptors on the release of norepinephrine and gamma-aminobutryic acid (GABA) that have been linked to the etiology of these neuropsychiatric symptoms.

62. A recent study has also observed that galantamine appears to reduce the sleep disruption and insomnia in Alzheimer's Disease patients and to perform better in this regard than donepezil. It is not clear why galantamine works in this way, since the relationship between the cholinergic system and sleep patterns is not well understood (Ancoli-Israel, S., *et al.* "Effects of Galantamine Versus Donepezil on Sleep in Patients With Mild to Moderate Alzheimer Disease and Their Caregivers: A Double-Blind, Head-to-Head, Randomized Pilot Study," *Alzheimer Disease & Associated Disorders* 19:240-245 (Oct.-Dec. 2005)). One possible explanation is that galantamine has a shorter effective half-life than donepezil, and as a consequence, the levels of cholinesterase inhibition (and allosteric modulation) for a patient on galantamine are substantially reduced, as compared to a patient on donepezil. Whether this is the correct explanation or not, it is clear that benefits to an Alzheimer's patient's sleep were not expected from administration of a cholinesterase inhibitor in January 1986.

63. Another area of possible unexpected benefit is in disease progression. Preclinical studies within the last 10 years indicate that activation of nicotinic receptors can alter the processing of amyloid precursor protein (APP) to amyloid. Most neuropsychopharmacologists and clinicians focused on Alzheimer's Disease research now agree that this is the proximate cause of neurodegeneration in Alzheimer's Disease. Furthermore, pre-

clinical and epidemiologic studies suggest that activation of nicotinic receptors can have trophic or neuroprotective effects on neurons.

64. All of the approved acetylcholinesterase inhibitors will, to some degree, promote nicotinic receptor activity in the cortex. However, galantamine, with its positive allosteric modulation of nicotinic receptors, would be expected to promote nicotinic receptor activity to a relatively greater degree than those that simply act as cholinesterase inhibitors.

65. As a result, galantamine may turn out to provide not only symptomatic treatment for the cognitive decline in Alzheimer's Disease, but also to have promise in slowing or altering the progress of the disease. This question is difficult to investigate clinically, among other reasons because of the ethical constraints on long-term double-blinded studies. However, an open-label long term extension study on galantamine reported extended benefits for galantamine and concluded that "[t]ogether with findings from other studies, these results strengthen the argument for early diagnosis and treatment and support the hypothesis that AChEI treatment slows AD progression." (Raskind, M.A., *et al.*, "The Cognitive Benefits of Galantamine Are Sustained for at Least 36 Months," *Arch. Neurol.* 61:252-56 (2004).) As far as I am aware, neither a neurochemical link between neuronal nicotinic receptor stimulation and amyloid formation nor a possible benefit in retarding AD progression for improving cholinergic neurotransmission was ever suspected back in 1986.

July 27, 2006
Date

Joseph T. Coyle
Dr. Joseph T. Coyle

EXHIBIT A

CURRICULUM VITAE

Name: Joseph T. Coyle, M.D.

Address: 115 Mill Street, Belmont, MA 02478

Place of Birth: Chicago, Illinois

Marital Status: Married, 1968; Genevieve Sansoucy Coyle
Children: Peter Joseph, Andrew Jerome and David Sansoucy

Education:

1965 A.B.	in cursu honoris cum laude; College of the Holy Cross
1969 M.D.	The Johns Hopkins University School of Medicine

Postdoctoral Training:

Internship and Residencies:

1969-1970	Intern in Pediatrics, The Johns Hopkins Hospital
1973-1976	Resident in Psychiatry, The Johns Hopkins Hospital

Research Fellowships:

1970-1973	Research Associate, Laboratory of Clinical Science, National Institute of Mental Health (Dr. Julius Axelrod), Bethesda, Maryland
2001	Neurobiology, Marine Biological Laboratory, Woods Hole, MA

Licensure and Certification:

1970	Maryland License Registration D15842 (inactive)
1970	Diplomate - National Board of Medical Examiners
1980	Board Certified in Psychiatry by the American Board of Psychiatry and Neurology
1991	Massachusetts License Registration 75163

Academic Appointments:

1974-1976	Assistant Professor of Pharmacology, The Johns Hopkins University School of Medicine
1976-1978	Assistant Professor of Pharmacology and Psychiatry, The Johns Hopkins University School of Medicine
1978-1980	Associate Professor of Pharmacology and Psychiatry, The Johns Hopkins University School of Medicine
1980-1991	Professor of Neuroscience, Psychiatry and Pharmacology, The Johns Hopkins University School of Medicine
1982-1991	Director: Division of Child Psychiatry, Professor of Psychiatry, Neuroscience, Pharmacology and Pediatrics, The Johns Hopkins University School of Medicine
1985-1991	Distinguished Service Professor of Child Psychiatry, The Johns Hopkins

Academic Appointments continued:

	University School of Medicine
1991-2001	Chair of the Consolidated Department of Psychiatry, Harvard Medical School
1991-	Eben S. Draper Professor of Psychiatry and of Neuroscience, Harvard Medical School

Endowed Lectureships and Major Visiting Appointments:

1981	Smith, Kline and French Visiting Professor, Flinders University and University of New South Wales, Australia
1983	Harold C. Voris Memorial Lecturer in Neuroscience, Mercy Hospital, University of Illinois School of Medicine, Chicago
1983	Grass Lecturer, University of Missouri School of Medicine
1986	Dean's Lecture, The Johns Hopkins School of Medicine
1987	Sterling Drug Visiting Professor, Department of Pharmacology, Medical College of Virginia
1987	Pfizer Visiting Professor of Psychiatry, Columbia University College of Physicians and Surgeons
1987	Tarbox Distinguished Neuroscientist Lecturer, Texas Tech University
1987	Grass Lecturer, University of South Carolina School of Medicine
1988	Nielson Lecture, University of Utah School of Medicine
1989	Centennial Visiting Professor, Celebration of the Sciences Lecturer, Washington College
1989	Dean's Distinguished Lecture, University of Colorado School of Medicine
1989	Halbert Robinson Distinguished Lecturer, University of North Carolina School of Medicine
1991	Axelrod Lecturer, City College of New York
1991	Gerard Symposium, University of Michigan
1992	Meyerowitz Lecturer, University of Rochester
1993	Andrew Woods Visiting Professorship and Lecture, University of Iowa
1993	Harvey Shein Lecture, American Association Psychiatric Residency Training Directors
1993	John E. Whitmore Lecture, Baylor College of Medicine
1993	The Wesco Lecture, University of Kansas School of Medicine
1993	Thomas Salmon Lecture, New York Academy of Medicine
1993	Jonathan Swift Psychiatric Lecture, St. Patrick's Hospital, Dublin, Ireland
1993	The Taylor Lecture in Neurology and Psychiatry, University of Maryland School of Medicine
1993	Pfizer Visiting Professor of Psychiatry, Allegheny General Hospital
1994	Adolf Meyer Lecture, American Psychiatric Association
1995	Guildea Lecture, Washington University School of Medicine
1995	Harold E. Cooper Lectureship, University of Texas Medical School
1995	Jonathan Cole Lectureship, St. Elizabeth's Hospital and Tufts University School of Medicine
1996	Ribicoff Lecture, Yale University School of Medicine
1996	Thomas L. O'Donohue Memorial Lecture in Neuropharmacology, Howard University College of Medicine
1997	Pfizer Visiting Professor of Psychiatry, University of North Carolina School of Medicine

Endowed Lectureships and Major Visiting Appointments continued:

1998	Seventy-Seventh Annual Beaumont Lecture, Wayne County Medical Society
1999	Stephen R. Max Memorial Lecture, University of Maryland School of Medicine
1999	Deane Lecture, Wellesley College
1999	Leo Kanner Lecture in Child and Adolescent Psychiatry, Johns Hopkins University School of Medicine
1999	Pfizer Visiting Professor of Psychiatry, Jefferson Medical College of Thomas Jefferson University
1999	Margaret Roche Donlon Bidwell Memorial Lecture, Massachusetts Institute of Technology
2000	The Distinguished Lecture in Neuroscience, University of Texas Medical School at Houston
2001	Kwin Finnegan Memorial Lectureship, University of Utah School of Medicine
2002	Lucile Packard Distinguished Lecture, Stanford University Medical Center
2002	The Twenty-Third Annual Alberto DiMascio Memorial Lecture, Tufts University School of Medicine
2005	Janssen Visiting Professor of Psychiatry, University of Washington School of Medicine
2005	Frederick G. Corneel Memorial Lecture, McLean Hospital

Awards and Honors:

1968-1969	Henry Strong Denison Research Scholarship
1969	Alpha Omega Alpha Student Research Award
1972	Fellowship for Third Study Program for Neurosciences Research Program, Boulder, Colorado
1977	Basil O'Connor Award from the March of Dimes
1977-1987	National Institute of Mental Health Research Career Development Award, Type II
1978	A.E.Bennett Award in Basic Science from the Society of Biological Psychiatry
1979	John Jacob Abel Award from the American Society of Pharmacology and Experimental Therapeutics
1979	Sato International Memorial Award from the Japanese Pharmaceutical Society
1982	Daniel Efron Award from the American College of Neuropsychopharmacology
1985	Foundations' Fund Prize for Research in Psychiatry, American Psychiatric Association
1985-1991	Javits Neuroscience Investigator Award, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health
1986	Alpha Omega Alpha Honor Society
1990	Nancy and Daniel Weisman Award for Research on Mental Retardation
1990	Institute of Medicine of the National Academy of Sciences
1991	Edward A. Strecker Award from the Institute of Pennsylvania Hospital
1991	The Gold Medal Award from the Society of Biological Psychiatry
1991-92	President, Society of Neuroscience
1992	William R. McAlpin, Jr. Research Achievement Award from the National Mental Health Association

Awards and Honors continued :

1994	Fellow, American Academy of Arts and Sciences
1995	Hilton Investigator Award from the National Alliance for Research on Schizophrenia and Depression
1996	Kempf Fund Award for Research Development in Psychobiological Psychiatry, American Psychiatric Association
1997	Robert J. and Claire Pasarow Foundation Award for Neuropsychiatric Research
1997	Exemplary Psychiatrist Award, National Alliance for the Mentally Ill
2001-02	President, American College of Neuropsychopharmacology
2001-04	Council, American Association for the Advancement of Science
2001	Highly Cited Researchers Award, ISI Thomson Scientific
2001	Society for Neuroscience, Special Achievement Award
2003	Organizer and Chairman (with C. Robert Cloninger) "Integrating Programs with Genetics and Neuropharmacology of Schizophrenia," Cold Spring Harbor Laboratory
2004	Lieber Prize, National Alliance for Research on Schizophrenia and Depression
2004	Society for Neuroscience, Award for "Lifelong Dedication to Excellence and Diversity in Neuroscience"
2005	Elected Fellow, American Association for the Advancement of Science

Major Committee Assignments:

National Institute of Mental Health:

1977-1981	Preclinical Psychopharmacology Research Review Committee Member
1982	Scientific Councillor for the Intramural Program, ad hoc
1985-1989	Cellular Neurobiology and Psychopharmacology Research Review Committee, Chairman
1985-1988	Extra-mural Scientific Advisory Board
1990-1994	National Advisory Mental Health Council
1995	Search Committee for NIMH Director

Institute of Medicine:

1988	Committee on Research on Children and Adolescents with Mental, Behavioral and Developmental Disorders
1989	Committee on a National Neural Circuitry Database
1992	Committee on Prevention of Mental Disorders
1993-1995	Membership Committee
1991-2000	Board of Biobehavioral Sciences and Mental Disorders
1994-2000	Chair, Board of Biobehavioral Sciences and Mental Disorders

The Johns Hopkins University School of Medicine:

1979-1991	Graduate Education Steering Committee, Department of Pharmacology
1979-1982	Member: Medical School Council
1981-1982	Vice Chairperson: Medical School Council
1981-1982	Member: Advisory Board to the School of Medicine
1990-1991	Pharmacy and Therapeutics Committee
1981-1991	Medical Scientist Training Program Steering Committee
1978-1982	Director: Interdisciplinary Postdoctoral Training Program in Neurosciences, MH-15330
1983-1986	Johns Hopkins University Press, Editorial Board

2002-2005 Working Group on Interspecific Chimeric Primate Brains

Major Committee Assignments continued:

Harvard Medical School:
1991-1994 Subcommittee of Professors
1991-1993 Committee of Professors
1991-1996 Harvard Medical Center, Board of Trustees
1992-1996 Graduate Medical Education Committee
1994-1995 HMS Research Council
1994 LCME Self Study Committee on Objectives, Chairman
1996 Search Committee for Dean Harvard Medical School

Memberships, Offices and Committee Assignments in Professional Societies:

Society for Neuroscience (Member 1975):
1980-1983 Program Committee
1986 Chairman of Program Committee, Washington, D.C. Meeting
1986-1988 Council
1988-1989 Treasurer
1989-1990 Council
1990-1991 President Elect
1991-1992 President
1995-2003 Chairman, Governmental and Public Affairs Committee
1995-2005 Deputy Director, Minority Neuroscience Fellowship Program

1975- American Society for Neurochemistry

American Association for the Advancement of Science
2001-2004 Neuroscience Section: Council Delegate
2001-2004 Council Affairs Committee

American Psychiatric Association (Member 1976):
1990-2003 Fellow
2003- Distinguished Fellow
1986-1990 Scientific Advisory Panel
2000- Institute for Research and Education Scientific Advisory Panel
1976- Sigma Xi

1978- American Society for Pharmacology and Experimental Therapeutics

Collegium Internationale Neuropsychopharmacologicum (Member 1978):
1997-1998 Nominating Committee
2001-2004 Program Committee

American College of Neuropsychopharmacology (Member 1979, Fellow 1997)
1989-1991 Finance Committee
1991 Awards Committee
1991- Journal Editorial Board- Neuropsychopharmacology
1993 Outreach Task Force
1996-1998 Committee on Problems of Public Concern
1997-1999 Program Committee (Co-Chair)

1998-2001 Council
2001-2002 President

Memberships, Offices and Committee Assignments in Professional Societies continued:

2002-2004 Council
2004- Publication Committee (Co-Chair)

1980 National Foundation March of Dimes, Scientific Advisory Board, ad hoc
1981-1985 National Huntington's Disease Association National Medical and Scientific Advisory Council
1982-1986 Committee to Combat Huntington's Disease, Scientific Advisory Board
1982- International Society for Developmental Psychobiology
1982-1990 Hereditary Disease Foundation, Scientific Advisory Board

Alzheimer's Disease and Related Disorders Association
1982-1985 Scientific Advisory Board
1990-1992 Scientific Advisory Board

American Academy of Child and Adolescent Psychiatry (Member 1982):
1989-1992 Work Group on Research

1985-1988 International Rett's Syndrome Association, Professional Advisory Board
1988-1993; Pfizer Scholars Award, Advisory Board
1990-2003 John F. Merck Foundation, Scientific Advisory Board
1991- Massachusetts Hospital Association
1991- Massachusetts Psychiatric Society
1993-2001 Board of Trustees, McLean Hospital
1994- National Alliance for Autism Research Scientific Advisory Board
1995- Health Emotions Research Institute Scientific Advisory Board
1995- American College of Psychiatrists (Fellow)
1995- Dana Alliance for Brain Inititatives, Scientific Advisory Board
1996-1998 Hitchings-Elion Fellowships/Wellcome Research Travel Grant Advisory Committee
1996- International Academy for Biomedical and Drug Research
1996- Board of Trustees, Judge Baker Children's Center
2001- Marine Biological Laboratory Alumni Relations Advisory Board
2002-2004 Research Advisory Committee on Gulf War Veterans' Illnesses

Major Research Interest:

Signal Transduction in the Nervous System

Editorial Responsibilities:

1993-2003 Harvard Review of Psychiatry: Editor-in-Chief
2002- Archives of General Psychiatry: Editor-in-Chief

Editorial Boards:

1984- Journal of Developmental and Behavioral Pediatrics
1984- Developmental Brain Research
1984-1992 Neuropharmacology

1986-1992	European Journal of Pharmacology
1988-1993	The Journal of Neuroscience

Editorial Responsibilities Continued:

1988-	Molecular Psychiatry
1988-	Molecular and Chemical Neuropathology
1988-	Synapse
1989-	Archives of General Psychiatry
1989-1999	Metabolic Brain Disease
1990-	Journal of Neuroscience Research
2000-	Acta Paedopsychiatrica
1991-2000	Journal of Child and Adolescent Psychopharmacology
1991-	Neuropsychopharmacology
1992-1998	Advances in Pharmacology
1992-1998	Oxford University Press Psychiatry Series
1992-	Neurobiology of Disease
1993-	Cerebral Cortex
1993-2000	Current Opinion in Psychiatry
1994-	Neuroscience
1994-	Journal of Psychiatric Research
1995-2001	American Psychiatric Press, Inc.
1996-	Acta Paedopsychiatrica, International Journal of Child and Adolescent Psychiatry
1996-2002	Journal Watch for Psychiatry
1997-2001	American Journal of Psychiatry
1999-	Journal of Molecular Neuroscience
2002-	Journal of the American Medical Association

Advisory Boards:

1978-1981	Developmental Neurosciences
1979-	Life Sciences
1983-	Neurobehavioral Toxicology
1984-1993	Neurobiology of Aging
1991-	CRC Critical Reviews in Neurobiology
1992-1996	Cambridge Series in Psychopharmacology
1995-	Current Protocols in Pharmacology
1999-	The Autism Brain Library Trust

Doctoral Students and Titles of Theses:

Kathleen Bizière, M.D., Ph.D. (1978) "Etude d'un modèle animal de la Chorée de Huntington"
Michael McKinney, Ph.D. (1982) "Cholinergic Innervation of the Mammalian Cerebral Cortex and Hippocampus by the Basal Forebrain: Implications for Senile Dementia of the Alzheimer Type"
Alfred Malouf, Ph.D. (1983) "The Regulation of [3H]Glutamic Acid Binding Sites on N18-RE-105 Neuroblastoma Hybrid Cells in Culture"
Kerry Koller, Ph.D. (1984) "The Purification and Pharmacologic Characterization of N-Acetyl-Aspartyl-Glutamate, a Possible Excitatory Neurotransmitter"
Robert Zaczek, Ph.D. (1986) "Characterization of a Novel Brain Specific Chloride Dependent Glutamic Acid Transport"
Randy D. Blakely, Ph.D. (1987) "N-Acetyl-Aspartyl-Glutamate: The Elucidation of Specific Catabolic and Anatomic Pathways in the Rat CNS"
Timothy H. Murphy, Ph.D. (1989) "Glutamate Toxicity in a Neuronal Cell Line Involves Inhibition of Cystine Uptake Leading to Oxidative Stress"
Mario D. Saltarelli, M.D., Ph.D. (1989) "Studies on the Regulation of High-Affinity Choline Uptake"
Joanne E. Sweeney, Ph.D. (1989) "Developmental, Neurochemical and Functional Properties of the Cholinergic Basal Forebrain Complex in Mice"
Barbara Stauch Slusher, Ph.D. (1991) "Purification, Antibody Production, and Immunocytochemical Localization of Rat Brain N-Acetylated α-Linked Acidic Dipeptidase (NAALADase)"
Guochuan Tsai, M.D., Ph.D. (1991) "Anatomy, Physiology and Pathophysiology of N-Acetylaspartylglutamate"
Carter, Ruth, Ph.D. (1997) "Cloning and Expression of the Naladase Neuropeptidase"
Passani, Lucius, Ph.D. (1997) "Distribution of N-acetylaspartylglutamate and N-acetylated Alpha Linked Acidic Dipeptidase in Human Brain and the Effects of Disease Related and Induced Neuronal Degeneration"
Schwartz, Paul J., Ph.D. (1998) "Effect of Altered Expression of the Cytoplasmic Copper-Zinc Superoxide Dismutase on Oxidative Stress Mediated Phenomena: Implications for Down's Syndrome and Glutamate Neurotoxicity"

Post-doctoral Fellows and Current Positions:

Robert Schwarcz, Ph.D., 1976-78, Professor of Psychiatry and Pharmacology, University of Maryland School of Medicine
Edythe London, Ph.D., 1978-80, Professor of Psychiatry, UCLA
John Slevin, M.D., 1979-81, Professor of Neurology, University of Kentucky
Michele Beaulieu, Ph.D., 1980-82, Hoffman-LaRoche
Michael Johnston, M.D., 1980-82, Professor of Neurology, Johns Hopkins
Larry Tune, M.D., 1980-82, Professor of Psychiatry, Emory University
Peter Campochiaro, M.D., 1982-83, Professor of Opthalmology, Johns Hopkins
Paul Sanberg, Ph.D., 1982-84, Professor of Neurosurgery, University of Florida Medical School
John Lehmann, Ph.D., 1983-85, Associate Professor of Neuroscience, Hahnemann Medical School
Pedro Lowenstein, M.D., Ph.D., 1985-87, Professor of Neuroscience, University of California, Los Angeles
Michael Robinson, Ph.D., 1986-89, Associate Professor of Pediatrics and Pharmacology, University of Pennsylvania School of Medicine
Giancarlo Forloni, Ph.D., 1986-88, Mario Negri Institute, Milan
Piero Antuono, M.D., 1985-87, Associate Professor of Neurology, Medical College of Wisconsin

Post-doctoral Fellows and Current Positions Continued:

Carla Bendotti, Ph.D., 1986-88, Mario Negri Institute, Milan
Christine Hohmann, Ph.D., 1987-90, Professor of Biology, Morgan State University
George Capone, M.D., 1988-90, Associate Professor of Pediatrics, Johns Hopkins
Pamela Puttfarcken, Ph.D., 1989-92, Scientist, Abbott Laboratories
Maria Caserta, M.D., Ph.D., 1989-91, Associate Professor of Psychiatry, Northwestern University School of Medicine
Urs Berger, Ph.D., 1992-94, Instructor in Psychiatry, Harvard Medical School
Guochuan Tsai, M.D., Ph.D., 1994-95, Assistant Professor of Psychiatry, Harvard Medical School
Richard Bergeron, M.D., Ph.D., 1995-2000, Assistant Professor of Psychiatry, University of Ottawa School of Medicine
Cecelia Flores, Ph.D., 2000-2002, Instructor, Montreal Neurological Institute
Jonathan Pickar, M.D., Ph.D., 2003-, Instructor in Medicine, Harvard Medical School
Alo Basu, Ph.D., 2005-, Research Fellow, Harvard Medical School
Amy Lawson-Yuen, M.D., Ph.D., 2005- Fellow, Harvard Medical School

Employment Resumé:

Dr. Coyle was appointed an Assistant Professor of Pharmacology while a Resident in Psychiatry at Johns Hopkins Medical School in 1974. Four years after completing his Residency in Psychiatry, he was promoted to the rank of Professor of Pharmacology and of Psychiatry in 1980.

In 1981, he was named Professor and Director of the Division of Child and Adolescent Psychiatry at Johns Hopkins. At the time, the Division consisted of four junior faculty members, had no external research support, trained one to two residents per year and provided care in outmoded facilities. During his nine years as Director, the Division developed 26 bed inpatient service for child and adolescent patients, increased the Residency Training Program to five positions per year, expanded to ten faculty members and attracted nearly $2MM per year in grant and contract support. Several faculty then recruited to the Division now hold leadership positions at their institutions including the Directors of the Division of Child and Adolescent Psychiatry at Stanford (A. Reiss, M.D.), at George Washington (P. Joshi, M.D.) and at Jefferson (G. Edelsohn, M.D., M.P.H.) and the Director of the Mental Retardation Research Institute of the University of North Carolina (J. Piven, M.D.).

In 1991, he was recruited to Harvard Medical School to serve as the Chairman of five of its nine affiliated programs in Psychiatry. In three years, the remaining affiliated programs in Psychiatry joined the Consolidated Department of Psychiatry, making it the only academically unified major clinical department at Harvard Medical School. The Department contained over 1500 part-time and full-time faculty and has nearly 200 residents in adult and child psychiatry in training. He reorganized residency training, condensing six competing adult residency training programs into three thematically differentiated programs with a single application form. The six child psychiatry residencies were merged into three with a single core curriculum. The Medical Student curriculum, historically dependent on idiosyncrasies of the nine hospital departments, was reorganized with clear objectives so that all students could be subject to the same tests of their knowledge. He focused on the career development of women, resulting in substantial increases in women's representation at the assistant and associate professor levels and a four-fold increase in women professors. Between 1991 and 2001, the external funding for the components of the Consolidated Department of Psychiatry grew from less than $20 MM to over $65MM. Through outreach efforts with the Department of Mental Health of the State of Massachusetts, the Consolidated Department of Psychiatry received an annual grant of nearly $3MM per year to support residency education in Psychiatry. In addition, the Department received $2.2 MM per year from the State for a 12-bed inpatient unit to carry out clinical research on severe mental illness. He stepped down as Chairman in 2001 after ten years and holds the Eben S. Draper Chair of Psychiatry and Neuroscience.

Dr. Coyle's research in neuroscience has been continuously funded by NIH since 1975, and he currently serves as the Director of a $7 MM NIMH Conte Center on the Neurobiology of Schihzophrenia. He has also played a national leadership role in Neuroscience and Psychiatry. He served as Councilor, Treasurer and ultimately President (1991-92) of the Society for Neuroscience, an international scientific organization with over 30,000 members. He served on an NIMH Initial Review Group (IRG) for eight years, four of which he was the chairman. He also served on the National Advisory Council to NIMH (1990-94). Elected to the Institute of Medicine in 1990, he chaired the Board of Neuroscience and Behavioral Health (1994-2000). He was president of the American College of Neuropsychopharmacology (ACNP), a leading honorific society in Psychiatry, in 2002. He sits on the editorial advisory boards of over twenty journals including *JAMA* and is the editor-in-chief of the *Archives of General Psychiatry* . He was elected a fellow of the American Academy of Arts and Sciences and of the American Association for the Advancement of Science

BIBLIOGRAPHY

Text Books

1. S.J. Enna and J.T. Coyle, Eds. ***Neuroleptics: Neurochemical, Behavioral and Clinical Perspectives,*** Raven Press, New York, 1983.

2. J.T. Coyle, Ed. ***Animal Models of Dementia: A Synaptic Neurochemical Perspective***, Alan R. Liss, Inc., New York, 1987.

3. R.S. Fisher and J.T. Coyle, Eds. ***Neurotransmitters and Epilepsy: Frontiers of Clinical Neuroscience, Vol. 11,*** Wiley-Liss, Inc., New York, 1991.

4. K. Davis, H. Klar and J.T. Coyle, Eds. ***Foundations of Psychiatry*** , W.B. Saunders, Philadelphia, 1991.

5. D.L. Schacter (Ed.) J.T. Coyle, G.D. Fischbach, M-M Mesulam and L.E. Sullivan. (Co-Eds.) ***Memory Distortion: How Minds, Brains, and Societies Reconstruct the Past.*** Harvard University Press, Cambridge, 1995.

6. S.J. Enna and J.T. Coyle, Eds. ***Pharmacological Management of Neurological and Psychiatric Disorders,*** McGraw-Hill, New York, 1998.

7. K.L.Davis, D. Charney, J.T. Coyle and C. Nemeroff, Eds. ***Neuropsychopharmacology: The Fifth Generation of Progress***. Lipincott, Williams and Wilkins, Philadelphia, 2002.

Original Reports

1. S.H. Snyder and J.T. Coyle. Regional differences in [3H]-norepinephrine and [3H]-dopamine uptake into rat brain homogenates. J. Pharmacol. Exp. Therap. 165:78-86, 1969.

2. J.T. Coyle and S.H. Snyder. Catecholamine uptake by synaptosomes in homogenates of rat brain: stereospecificity in different areas. J. Pharmacol. Exp. Therap. 170:221-231, 1969.

3. J.T. Coyle and S.H. Snyder. Antiparkinsonian drugs: inhibition of dopamine uptake in the corpus striatum as a possible mechanism of action. Science 166:899-901, 1969.

4. S.H. Snyder, K.M. Taylor, J.T. Coyle and J.L. Meyerhoff. The role of brain dopamine in behavioral regulation and actions of psychotropic drugs. Am. J. Psychiatry 127:117-125, 1970.

6. A.S. Horn, J.T. Coyle and S.H. Snyder. Catecholamine uptake by synaptosomes from Rat brain; structural activity relationships of drugs with differential effects on dopamine and norepinephrine neurons. Mol. Pharmacol. 7:66-80, 1971.

6. J.T. Coyle and J. Axelrod. Development of uptake and storage of L-[3H]-norepinephrine in the rat brain. J. Neurochem. 18:2061-2075, 1971.

7. J.T. Coyle and J. Axelrod. Dopamine-beta-hydroxylase in rat brain:developmental characteristics. J. Neurochem. 19:449-459, 1972.

8. J.T. Coyle. Tyrosine hydroxylase in rat brain: cofactor requirements, regional and subcellular distribution. Biochem. Pharmacol. 21:1935-1944, 1972.

9. J.T. Coyle and J. Axelrod. Tyrosine hydroxylase in rat brain: developmental characteristics. J. Neurochem. 19:1117-1123, 1972.

10. F. Lamprecht and J.T. Coyle. Dopa decarboxylase in developing rat brain. Brain Res. 1:503-506, 1972.

11. J.T. Coyle and G.F. Wooten. Rapid axonal transport of tyrosine hydroxylase and dopamine-beta-hydroxylase. Brain Res. 44:701-704, 1972.

12. J.M. Saavedra, J.T. Coyle and J. Axelrod. The distribution and properties of the nonspecific N-methyl-transferase in brain. J. Neurochem. 20:743-752, 1973.

13. G.F. Wooten and J.T. Coyle. Axonal transport of catecholamine synthesizing and metabolizing enzymes. J. Neurochem. 20:1361-1371, 1973.

14. J.T. Coyle and D. Henry. Catecholamines in fetal and newborn rat brain. J. Neurochem. 21:61-67, 1973.

15. J.T. Coyle, D. Jacobwitz, D. Klein and J. Axelrod. Dopaminergic neurons in explants of sustantia nigra in culture. J. Neurobiol. 4:461-470, 1973.

16. J.T. Coyle, P. Wender and A. Lipsky. Avoidance conditioning in different strains of rats: neurochemical correlates. Psychopharmacologia (Berl.) 31:25-34, 1973.

17. J.T. Coyle and M.J. Kuhar. Subcellular localization of dopamine-beta-hydroxylase and endogenous norepinephrine in rat hypothalamus. Brain Res. 65:475-487, 1974.

18 J.T. Coyle, G.F. Wooten and J. Axelrod. Evidence for extra noradrenergic dopamine-beta-hydroxylase activity in rat salivery gland. J. Neurochem. 22:923-930, 1974.

19. J.M. Saavedra, J.T. Coyle and J. Axelrod. Developmental characteristics of phenylethanolamine and octopamine in the rat brain. J. Neurochem. 23:511-515, 1974.

20. R.W. Holz and J.T. Coyle. The effects of various salts, temperature and the alkaloids veratridine and batrachotoxin on the uptake of [3H]-dopamine into synaptosomes from rat striatum. Mol. Pharmacol. 10:746-758, 1974.

21. J.T. Coyle and S.J. Enna. Neurochemical aspects of the ontogenesis of GABAergic neurons in the rat brain. Brain Res. 111:119-133, 1976.

22. J.T. Coyle and P. Campochiaro. Ontogenesis of dopaminergic-cholinergic interactions in the rat striatum: A neurochemical study. J. Neurochem. 27:673-678, 1976.

23. J.T. Coyle and C.B. Pert. Ontogenetic development of [3H]Naloxone binding in rat brain. Neuropharmacology 15:555-560, 1976.

24. R. Schwarcz and J.T. Coyle. Adenylate cyclase activity in chick retina. Gen. Pharmacol.

7:349-354, 1976.

25. J.T. Coyle and H.I. Yamamura. Neurochemical aspects of the ontogenesis of cholinergic neurons in the rat brain. Brain Res. 118:429-440, 1976.

26. R. Grzanna and J.T. Coyle. Rat adrenal dopamine-beta-hydroxylase: purification and immunologic characteristics. J. Neurochem. 27:1091-1096, 1976.

27. J.T. Coyle and R. Schwarcz. Lesion of striatal neurones with kainic acid provides a model for Huntington's chorea. Nature 263:244-246, 1976.

28. R. Schwarcz and J.T. Coyle. Striatal lesions with kainic acid: neurochemical characteristcs. Brain Res. 127:235-249, 1977.

29. J.T. Coyle and M.E. Molliver. Major innervation of newborn rat cortex by monoaminergic neurons. Science 196:444-447, 1977.

30. R. Schwarcz, J.P. Bennett and J.T. Coyle. Loss of striatal serotonin synaptic receptor binding induced by kainic acid lesion: correlations with Huntington's Disease. J. Neurochem. 28:867-869, 1977.

31. R. Schwarcz and J.T. Coyle. Kainic acid: Neurotoxic effects after intraocular injection. Invest. Ophthalmol. 16:141-149, 1977.

32. R. Grzanna, J. Morrison, J.T. Coyle and M.E. Molliver. Major improvements in the immunohistochemical demonstrations of noradrenergic neurons in the rat brain. Neurosci. Lett. 4:127-134, 1977.

33. R. Schwarcz and J.T. Coyle. Neurochemical sequelae of kainate injections in corpus striatum and substantia nigra of the rat. Life Sci. 20:431-436, 1977.

34. J.T. Coyle, R. Schwarcz, J.P. Bennett and P. Campochiaro. Clinical, neuropathologic and pharmacologic aspects of Huntington's Disease: Correlates with a new animal model. Prog. Neuropsychopharmacology.1:13-30, 1977.

35. R. Grzanna and J.T. Coyle. Immunochemical studies on the turnover of rat serum dopamine beta-hydroxylase. Mol. Pharmacol. 13:956-964, 1977.

36. P. Campochiaro, R. Schwarcz and J.T. Coyle. GABA receptor binding in rat striatum: Localization and effects of denervation. Brain Res. 136:501-511, 1977.

37. R. Schwarcz, J.P. Bennett, and J.T. Coyle. Inhibitors of GABA metabolism: implications for Huntington's disease. Ann. Neurol. 2:299-303, 1977.

38. F. Garcin and J.T. Coyle. Effects of perinatal 6-hydroxydopamine treatment on opiate receptor distribution in adult brain. Psychopharmacol. Comm. 1:283-290, 1977.

39. R.M. Herndon and J.T. Coyle. Selective destruction of neurons by a transmitter agonist. Science 198:71-72, 1977.

40. R. Schwarcz, D. Scholz and J.T. Coyle. Structure-activity relations for the neurotoxicity of kainic acid derivatives and glutamate analogues. Neuropharmacology. 17:145-151, 1978.

41. Schwarcz, I. Creese, J.T. Coyle and S.H. Snyder. Dopaminergic receptor Localization in rat corpus striatum: differential effects of kainic acid lesion and cerebral cortex ablation of dopamine-sensitive adenylate cyclase and [3H]-haloperidol binding. Nature 271, 766-768, 1978.

42. J.T. Coyle, M.E. Molliver and M.J. Kuhar. In situ injection of kainic acid: A new method for selectively lesioning neuronal cell bodies while sparing axons of passage. J. Comp. Neurol. 180:301-323, 1978.

43. J.H. Morrison, R. Grzanna, M.E. Molliver and J.T. Coyle. The distribution and orientation of noradrenergic fibers in neocortex of the rat: an immunofluorescence study. J. Comp. Neurol. 181:17-40, 1978.

44. R. Grzanna and J.T. Coyle. Dopamine-beta-hydroxylase in rat submandibular ganglion cells which lack norepinephrine. Brain Res. 151: 206-214, 1978.

45. P. Campochiaro and J.T. Coyle. Ontogenetic development of kainate neurotoxicity: correlates with glutamatergic innervation. Proc. Natl. Acad. Sci. USA 75:2025-2029, 1978.

46. K. Biziere and J.T. Coyle. Effects of kainic acid on ion distribution and ATP levels of striatal slices incubated *in vitro*. J. Neurochem. 31:513-520, 1978.

47. R. Zaczek, R. Schwarcz and J.T. Coyle. Long-term sequelae of striatal kainate lesion. Brain Res. 152:626-632, 1978.

48. R. Grzanna, M.E. Molliver and J.T. Coyle. Golgi-like demonstration of central noradrenergic neurons in thick sections by the unlabeled antibody method. Proc. Natl. Acad. Sci. USA 75:2502-2506, 1978.

49. R.E. Hruska, R. Schwarcz, J.T. Coyle and H.I. Yamamura. Alterations of muscarinic cholinergic receptors in the rat caudate nucleus after kainic acid injections. Brain Res. 152:620-625, 1978.

50. K. Biziere and J.T. Coyle. Influence of cortico-striatal afferents on striatal kainic acid neurotoxicity. Neurosci. Lett. 8:303-310, 1978.

51. E.D. London and J.T. Coyle. Pharmacological augmentation of acetylcholine levels in kainate-lesioned rat striatum. Biochem. Pharmacol. 27:2962-2965, 1978.

52. R. Schwarcz, R. Zaczek and J.T. Coyle. Microinjection of kainic acid into the rat hippocampus. Eur. J. Pharmacol. 50:209-220, 1978.

53. R. Grzanna and J.T. Coyle. Absence of a relationship between sympathetic neuronal activity and turnover of serum dopamine-beta-hydroxylase. N.S. Arch. Pharmacol. 304:231-236, 1978.

54. J.T. Coyle. An animal model for Huntington's disease. J. Biol. Psychiatry 14:251-276, 1978.

55. E.D. London, L.W. Harris, W.C. Heyl and J.T. Coyle. Effect of 2-dimethylamino-ethanol in kainate-lesioned rat striatum: anomaly in the radioenzymatic assay of acetylcholine. Communications in Psychopharmacology 2:357-364, 1978.

56. W. Sieghart, J. Forn, R. Schwarcz, J.T. Coyle and P. Greengard. Neuronal localization of specific brain phosphoproteins. Brain Res. 156:345-350, 1978.

57. R. Zaczek, M.F. Nelson and J.T. Coyle. Effects of Anaesthetics and Anticonvulsants on the Action of Kainic Acid in the Rat Hippocampus. Eur. J. Pharmacol. 52:323-327, 1978.

58. M.V. Johnston, R. Grzanna and J.T. Coyle. Methylazoxymethanol treatment of fetal rats results in abnormally dense noradrenergic innervation of neocortex. Science 203:369-371, 1979.

59. M.R. DeLong and J.T. Coyle. Globus pallidus lesions in the monkey produced by kainic acid: histologic and behavioral effects. Appl. Neurophysiol. 42:95-97, 1979.

60. M.V. Johnston and J.T. Coyle. Histological and neurochemical effects of fetal treatment with methylazoxymethanol on rat neocortex in adulthood. Brain Res. 170:135-155, 1979.

61. E.D. London and J.T. Coyle. Specific binding of [3H]-kainic acid to receptor sites in rat brain. Mol. Pharmacol. 15:492-505, 1979.

62. R. Grzanna, M.F. Nelson, R.M. Weinshilboum, J. Dunnette and J.T. Coyle. Characterization of the basis for differences in serum DBH activity in immature and adult rats by use of homologous antibody. J. Neurochem. 33:913-922, 1979.

63. K. Biziere and J.T. Coyle. Localization of receptors for kainic acid on neurons in the innernuclear layer of retina. Neuropharmacology 18:409-413, 1979.

64. R. Zaczek, J.C. Hedreen and J.T. Coyle. Evidence for a hippocampal-septal glutamatergicpathway in rat. J. Exp. Neurol. 65:145-156, 1979.

65. E.D. London and J.T. Coyle. Cooperative interactions at [3H]-kainic acid binding sites in rat and human cerebellum. Eur. J. Pharmacol. 56:287-290, 1979.

66. R.G. Robinson and J.T. Coyle. Lateralization of catecholaminergic and behavioral response to cerebral infarction in the rat. Life Sci. 24:943-950, 1979.

67. L.E. Tune, I. Creese, J.T. Coyle, G. Pearlson and S.H. Snyder. Low neuroleptic serum levels in patients receiving fluphenazine decanoate. Am. J. Psychiatry, 137:80-82, 1979.

68. K. Biziere and J.T. Coyle. Effects of cortical ablation on the neurotoxicity and receptor binding of kainic acid in striatum. J. Neurosci. Res. 4:383-398, 1979.

69. M.V. Johnston, M. McKinney and J.T. Coyle. Evidence for a cholinergic projection to neocortex from neurons in the basal forebrain. Proc. Natl. Acad. Sci. USA 76:5392-5396, 1979.

70. B. Meyers, L.E. Tune and J.T. Coyle. Clinical response and serum neuroleptic levels in childhood schizophrenia. Am. J. Psychiatry, 137:483-484, 1979.

71. L. Tune and J.T. Coyle. Serum levels of anticholinergic drugs in the management of neuroleptic-induced acute extrapyramidal side-effects. Arch. Gen. Psychiatry 37:293-297, 1979.

72. J.H. Morrison, M.E. Molliver, R. Grzanna and J.T. Coyle. Noradrenergic innervation

Developmental Neuroscience 5:3-12, 1982.

103. K.C. Retz and J.T. Coyle. Effects of kainic acid on high energy metabolites in the mouse striatum. J. Neurochem. 38:196-203, 1982.

104. R. Zaczek and J.T. Coyle. Excitatory amino acid analogues: neurotoxicity and seizures. Neuropharmacology 21:15-26, 1982.

105. M. McKinney and J.T. Coyle. Regulation of neocortical muscarinic receptors: effects of drug treatment and lesions. J. Neurosci. 2:97-105, 1982.

106. H.S. Singer, J.T. Coyle, D.L. Weaver, N. Kawamura and H.J. Baker. Neurotransmitter chemistry in feline GM-1 gangliosidosis: a model for human ganglioside storage disease. Ann. Neurol. 12:37-41, 1982.

107. P.J. Whitehouse, D.L. Price, R.G. Struble, A.W. Clark, J.T. Coyle and M. DeLong. Alzheimer's disease and senile dementia: loss of neurons in the basal forebrain. Science 215:1237-1239, 1982.

108. L.E. Tune, M.E. Strauss, M.F. Lew, E. Breitlinger and J.T. Coyle. Serum levels of anticholinergic drugs and impaired recent memory in chronic schizophrenic patients. Am. J. Psychiatry 139:1460-1462, 1982.

109. H.S. Singer, I.J. Butler, L.E. Tune, W.E. Seifert and J.T. Coyle. Dopamine dysfunction in Tourette syndrome. Ann. Neurol., 12:361-366, 1982.

110. J.W. Ferkany, R. Zaczek and J.T. Coyle. Kainic acid stimulates excitatory amino acid neurotransmitter release at presynaptic receptors in the cerebellum. Nature 298:757-759, 1982.

111. J. Slevin, J. Collins, K. Lindsley and J.T. Coyle. Specific binding of [3H]-L-glutamate to cerebellar membranes: evidence for recognition site heterogeneity. Brain Res. 249:353-360, 1982.

112. M.V. Johnston, R. Haddad, A. Carman-Young and J.T. Coyle. Neurotransmitter chemistry of lissencephalic cortex induced in ferrets by fetal treatment with methylazoxymethanol acetate. Developmental Brain Research 4:285-291, 1982.

113. M. McKinney, R.G. Struble, D.L.Price and J.T. Coyle. Monkey nucleus basalis is enriched with choline actyltransferase. Neuroscience 7: 2363-2368, 1982.

114. J.W. Ferkany, J.T. Slevin, R. Zaczek and J.T. Coyle. Failure of folic acid derivatives to mimic the actions of kainic acid in brain *in vitro* or *in vivo*. Neurobehavioral Toxicology and Teratology 4:573-579, 1982.

115. K.C. Retz, A.C. Young and J.T. Coyle. Glutamate stimulation of ^{45}Ca uptake by rat striatal synaptosomes. Eur. J. Pharmacol. 79:319-322, 1982.

116. M. Beaulieu and J.T. Coyle. Fetally-induced noradrenergic hyperinnervation of cerebral cortex results in persistent down-regulation of beta-receptors. Developmental Brain Research, 4:491-494, 1982.

117. M. McKinney, P. Davies, and J.T. Coyle. Somatostatin is not co-localized in cholinergic neurons innervating the rat cerebral cortex-hippocampal formation. Brain Res. 243:169-172, 1982.

118. J.C. Harris, L.E. Tune, M. Kurtz, and J.T. Coyle. Neuroleptic serum levels in mentally retarded boys. Psychopharmacol. Bull. Vol. 18, 65-66, 1982.

119. D.L. Price, P.J. Whitehouse, R.G. Struble, A.W. Clark, J.T. Coyle, M.R. DeLong and J.C. Hedreen. Basal forebrain cholinergic systems in Alzheimer's Disease and related dementias. Neurosci. Commentaries 1:84-92, 1982.

120. G.R. Uhl, M. McKinney, J.C. Hedreen, C.L. White, III, J.T. Coyle, P.J. Whitehouse and D.L. Price. Dementia pugilistica: loss of basal forebrain cholinergic neurons and cortical cholinergic markers. Ann. Neurol. 12:99, 1982.

121. R. Zaczek, K. Koller, R. Cotter, D. Heller and J.T. Coyle. N-acetyl-aspartyl glutamate: an endogenous peptide with high affinity for a glutamate receptor in brain. Proc. Natl. Acad. Sci. USA 80:1116-1119, 1983.

122. J.T. Coyle, D.L. Price, and M.R. DeLong. Alzheimer's Disease: a disorder of cortical cholinergic innervation. Science 219:1184-1190, 1983.

123. J.W. Ferkany and J.T. Coyle. Kainic acid selectively stimulates the release of endogenous excitatory acidic amino acids. J. Pharmacol. Exp. Ther. 225: 399-406, 1983.

124. J.T. Coyle. Neurotoxic action of kainic acid. Short review. J. Neurochem. 41:1-11, 1983.

125. J.T. Slevin, J.F. Collins and J.T. Coyle. Analogue interactions with the brain receptor labeled by [3H]-kainic acid. Brain Res. 265:169-172, 1983.

126. H.S. Singer, D. Weaver, M. Tiemeyer and J.T. Coyle. Synaptic chemistry associated with aberrant neuronal development in the reeler mouse. J. Neurochem. 41:874-881, 1983.

127. J.W. Ferkany and J.T. Coyle. Specific binding of [3H]-+2-amino-7-phosphono heptanoic acid to rat brain membranes *in vitro*. Life Sci. 33:1295-1305, 1983.

128. M. McKinney, J.T. Coyle and J.C. Hedreen. Topographic analysis of the innervation of the rat neocortex and hippocampus by the basal forebrain cholinergic system. J. Comp. Neurol. 217:103-121, 1983.

129. J.E. Granato, B.J. Stern, A. Ringel, A.H. Karim, A. Krumholz, J.T. Coyle and S. Adler. Neuroleptic malignant syndrome: successful treatment with dantrolene and bromocriptine. Ann. Neurol. 14:89-96, 1983.

130. P.R. Sanberg, T.H. Moran, K.L. Kubos, and J.T. Coyle. Automated measurement of stereotypic behavior in rats. Behav. Neurosci. 97:830-832, 1983.

131. J.W. Ferkany and J.T. Coyle. Evoked release of aspartate and glutamate: disparities between prelabeling and direct measurement. Brain Res. 278:279-282, 1983.

132. M. Beaulieu and J.T. Coyle. Postnatal development of aminergic projections to

frontal cortex: effects of cortical lesions. J. Neurosci. Res. 10:351-361, 1983.

133. J.T. Coyle, M. McKinney, M.V. Johnston, and J.C. Hedreen. Synaptic neurochemistry of the basal forebrain cholinergic projection. Psychopharmacol. Bull. 19:441-447, 1983.

134. J.T. Coyle, J.W. Ferkany and R. Zaczek. Kainic Acid: Insights from a neurotoxin into the pathophysiology of Huntington's Disease. Neurobehavioral Toxicology and Teratology. 5:617-624, 1983.

135. A.W. Deckel, R.G. Robinson, J.T. Coyle, and P.R. Sanberg. Reversal of long-term locomotor abnormalities in the kainic acid model of Huntington's disease by day 18 fetal striatal implants. Eur. J. Pharmacol. 93: 287-288, 1983.

136. J. Lehmann, P. Schaefer, J.W. Ferkany and J.T. Coyle. Quinolinic acid evokes [3H]-acetylcholine release in striatal slices: mediation by NMDA-type excitatory amino acid receptors. Eur. J. Pharmacol. 96:111-115, 1983.

137. J.M. Waud, D.W. Chan, H.M. Drew, M.J. Oropeza, M.S. Sucupira, B. Scheinin, G.M. Garrison, M. Mayo, E. Taylor, J. Stem, D. Graham, J.T. Coyle, J. Niebyl and H.N. Wagner, Jr. Clinical evaluation of two direct procedures for free thyroxin, and of free thyroxin index determined nonisotopically and by measuring thyroxin-binding globulin. Clin. Chem. 29:1908-1911, 1983.

138. J.T. Coyle, H. Singer, M. Beaulieu and M.V. Johnston. Development of central neurotransmitter-specified neuronal systems: implications for pediatric neuropsychiatric disorders. Acta. Neurol. Scand. 69:1-11, 1984.

139. H. Singer, L. Oshida and J.T. Coyle. CSF cholinesterase activity in Gilles de la Tourette's Syndrome. Arch. Neurol. 41:756-757, 1984.

140. K. Sandberg, I. Hanin, A. Fisher and J.T. Coyle. Selective cholinergic neurotoxin: AF64A's effects in rat striatum. Brain Res. 293:49-55, 1984.

141. K.C. Retz and J.T. Coyle. The differential effects of excitatory amino acids on $^{45}CaCl_2$ by slices from mouse striatum. Neuropharmacology 23:89-94, 1984.

142. K.J. Koller and J.T. Coyle. Characterization of the interactions of N-acetyl-aspartyl-glutamate with [3H]-L-glutamate receptors. Eur. J. Pharmacol. 98:193-199, 1984.

143. J.T. Coyle, H. Singer, M. McKinney and D. Price. Neurotransmitter specific alterations in dementing disorders: Insights from animal models. J. Psychiatric. Res. 18:501-512, 1984.

144. H.S. Singer, M. Tiemeyer, J.C. Hedreen, J. Gearhart, and J.T. Coyle. Morphologic and neurochemical studies of embryonic brain development in murine Trisomy 16. Dev. Brain Res. 15:155-166, 1984.

145. K. Koller, R. Zaczek and J.T. Coyle. N-acetyl-aspartyl glutamate: regional levels in rat brain and the effects of brain lesions as determined by a new HPLC method. J. Neurochem. 43:1136-1142, 1984.

146. K. Sandberg, P. Sanberg and J.T. Coyle. Effects of intrastriatal injections of the

cholinergic neurotoxin AF64A on spontaneous nocturnal locomotor behavior in therat. Brain Res. 299:339-343, 1984.

147. J. Ferkany, R. Zaczek, A. Markl and J.T. Coyle. Glutamate-containing dipeptides enhance specific binding at glutamate receptors and inhibit specific binding at kainate receptors in rat brain. Neurosci. Lett. 44:281-286, 1984.

148. L.A. Cates, V-S. Li, Z-S. Hu, J. Lehmann, J.T. Coyle and J.W. Ferkany. Excitatory amino acid receptor interactions of a novel alpha-phosphinic acid analogue of alpha-methylaspartic acid. J. Pharm. Sci. 73:1550-1553, 1984.

149. P. Campochiaro, J.W. Ferkany and J.T. Coyle. The dissociation of evoked release of [3H]-GABA and of endogenous GABA from chick retina in vitro. Exp. Eye Res. 39:299-305, 1984.

150. G.T. Smith, T.H. Moran, J.T. Coyle, M.J. Kuhar, T.L. O'Donahue and P. McHugh. Anatomical localization of cholecystokinin receptors to the pyloric sphincter. Am. J. Physiol. 246:127-130, 1984.

151. M. Tiemeyer, H.S. Singer, J.C. Troncosco, L.C. Cook, J.T. Coyle and D.L. Price. Synaptic neurochemical alterations associated with neuronal degeneration in a canine inherited cerebellar ataxia. J. Neuropathol. Exp. Neurol. 43:580-591, 1984.

152. J. Lehmann, R.G. Struble, P.G. Antuono, J.T. Coyle, L.C. Cork and D.L. Price. Regional heterogeneity of choline acetyltransferase activity in primate neocortex. Brain Res. 322:361-364, 1984.

153. K.J. Koller and J.T. Coyle. Ontogenesis of N-acetyl-aspartate and N-acetyl-aspartyl-glutamate in rat brain. Dev. Brain Res. 317:137-140, 1984.

154. K. Sandberg, P.R. Sanberg, I. Hanin, A. Fisher and J.T. Coyle. Cholinergic lesion of the striatum impairs acquisition and retention of a passive avoidance response. Behavi.Neurosci. 98:162-165, 1984.

155. E.D. London, M. McKinney, M. Dam, A. Ellis and J.T. Coyle. Decreased cortical glucose utilization after ibotenate lesion of the rat ventro-medial globus pallidus. J. Cereb. Blood Flow and Metab. 4:381-390, 1984.

156. P.R. Sanberg, J. Pevsner and J.T. Coyle. Parametric influences on catalepsy. Psychopharmacol. 82:406-408, 1984.

157. A.T. Malouf, R.L. Schnaar and J.T. Coyle. Characterization of a glutamic acid neurotransmitter binding site on neuroblastoma hybrid cells. J. Biol. Chem. 259:12756-12762, 1984.

158. A.T. Malouf, J.T. Coyle and R.L. Schnaar. Agonists and cations regulate the glutamic acid receptors on intact neuroblastoma hybrid cells. J. Biol. Chem. 259:12763-12768, 1984.

159. K.J. Koller and J.T. Coyle. Specific labeling of brain receptors with [3H]N-acetyl-aspartyl-glutamate. Eur. J. Pharmacol. 104:193-194, 1984.

160. L.T. Kucharski, P. Alexander, L. Tune and J.T. Coyle. Serum neuroleptic

concentrations and clinical response: a radioreceptor assay investigation of acutely psychotic patients. Psychopharmacology 82:194-198, 1984.

161. P.R. Sanberg, T.H. Moran, K.L. Kubos and J.T. Coyle. Automated Measurement of Rearing Behavior in Adult and Neonatal Rats. Behav. Neurosci. 98:743-746, 1984.

162. N. Bizzozero, L. Merlini and J.T. Coyle. Synthesis of C-analogues of kainic acids and their interaction with brain receptors. Il Farmaco - Edizione Scientifica 39:612-617, 1984.

163. K. Sandberg, R.L. Schnaar, M. McKinney, I. Hanin, A. Fisher and J.T. Coyle. AF64A: An active site directed irreversible inhibitor of choline acetyltransferase. J. Neurochem. 44:439-445, 1985.

164. J. Lehmann, J.W. Ferkany, P. Schaeffer and J.T. Coyle. Dissociation between the excitatory and "excitotoxic" effects of quinolinic acid analogs on the striatal cholinergic interneuron. J. Pharmacol. Exp. Ther. 232:873-882, 1985.

165. M. Maisami, B.H. Sohmer and J.T. Coyle. Combined use of tricyclic antidepressants and neuroleptics in the management of terminally ill children: a report on three cases. J. Am. Acad. Child Psychiatry, 4:487-489, 1985.

166. L. Tune, S. Gucker, M. Folstein, L. Oshida and J.T. Coyle. Cerebrospinal fluid acetylcholinesterase activity in senile dementia of the Alzheimer type. Ann. Neurol. 17:46-48, 1985.

167. M.E. Strauss, M.F. Lew, J.T. Coyle and L.E. Tune. Psychopharmacologic and clinical correlates of attention in chronic schizophrenia. Am. J. Psychiatry 142:497-499, 1985.

168. P. Campochiaro, J.W. Ferkany and J.T. Coyle. Excitatory amino acid analogs evoke release of endogenous amino acids and acetyl choline from chick retina in vitro. Vision Res. 25:1375-1386, 1985.

169. J. Bernstein, R.S. Fisher, R. Zaczek and J.T. Coyle. Dipeptides of glutamate and aspartate may be endogenous neuroexcitants in the rat hippocampal slice. J. Neurosci. 5:1429-1433, 1985.

170. K. Sandberg, R.L. Schnaar and J.T. Coyle. Method for the quantitation and characterization of the cholinergic neurotoxin, monoethylcholine mustard aziridinium ion (AF64A). J. Neurosci. Methods 14:143-148, 1985.

171. D.F. Gutterman, E.I. Correa, J.R. DePaulo and J.T. Coyle. RBC choline and renal disorders during lithium treatment. Am. J. Psychiatry 142:493-495, 1985.

172. D.J. Hepler, D.S. Olton, G.L. Wenk and J.T. Coyle. Lesions in nucleus basalis magnocellularis and medial septal area of rats produce qualitatively similar memory impairments. J. Neurosci. 5:866-873, 1985.

173. K. Sandberg and J.T. Coyle. Characterization of [3H]Hemicholinium-3 binding associated with neuronal choline uptake sites in rat brain membranes. Brain Res. 348:321-330, 1985.

174. G.A. Foster, T. Hokfelt, J.T. Coyle and M. Goldstein. Immunohistochemical

evidence for phenylethanolamine-N-methyltransferase-positive tyrosine hydroxylase-negative neurones in the retina and the posterior hypothalamus of the rat. Brain Res., 330:183-188, 1985.

175. K.J. Koller and J.T. Coyle. The characterization of the specific binding of [3H]-N-acetyl-aspartyl-glutamate to rat brain membranes. J. Neurosci. 5:2882-2888, 1985.

176. B. Knowlton, G.L. Wenk, D.S. Olton and J.T.Coyle. Basal forebrain lesions produce a dissociation of trial dependent and trial independent memory performance. Brain Res. 345:315-321, 1985.

177. D.J. Hepler, G.L. Wenk, B.L. Cribbs, D.S. Olton and J.T. Coyle. Memory impairments following basal forebrain lesions. Brain Res. 346:8-14, 1985.

178. J.M.H. ffrench-Mullen, K. Koller, R. Zaczek, J.T. Coyle, N. Hori and D.O. Carpenter. N-Acetylaspartylglutamate: possible role as the neurotransmitter of the lateral olfactory tract. Proc. Natl. Acad.Sci. USA 82:3897-3900, 1985.

179. P.K. Joshi, J. Capozzoli and J.T. Coyle. Case Report: Effective management with lithium of a persistent, post-traumatic hypomania in a 10 year old child. J. Dev. Behav. Pediatr. 6:352-354, 1985.

180. J.L. Meyerhoff, K.J. Koller, D.D. Walczak and J.T. Coyle. Regional brain levels of N-acetyl-aspartyl-glutamate: The effect of kindled seizures. Brain Res. 346:392- 399, 1985.

181. P.R. Sanberg, J. Pevsner, P.G. Antuono and J.T. Coyle. Fetal methylazoxy-methanol acetate-induced lesions cause reductions in dopamine receptor-mediated catalepsy and stereotypy. Neuropharmacology 24:1057-1062, 1985.

182. A.W. Clark, H.J. Manz, C.L. White, J. Lehmann, D. Miller and J.T. Coyle. Cortical degeneration with swollen chromatolytic neurons: its relationship to Pick's disease. J. Neuropathol. Exp. Neurol. 45:268-284, 1986.

183. P.K. Joshi, M. Maisami and J.T. Coyle. Prospective study of intake procedures in a child psychiatry clinic. J. Clin. Psychiatry, 47:111-113, 1986.

184. G. Jayaram, J.T. Coyle and L.E. Tune. Relapse in chronic schizophrenics treated with fluphenazine decanoate is associated with low serum neuroleptic levels. J. Clin. Psychiatry 47:247-248, 1986.

185. S.L. Hyman, J.T. Coyle, J.C. Parke, C. Porter, G.H. Thomas, W. Jankel and M.L. Batshaw. Anorexia andaltered serotonin metabolism in a patient with argininosuccinic aciduria. J. Pediatr. 108:705-709, 1986.

186. T.H. Moran, P.R. Sanberg, P.G. Antuono and J.T. Coyle. Methylazoxymethanol acetate cortical hypoplasia alters the pattern of stimulation-induced behavior in neonatal rats. Devel. Brain Res. 27:235-242, 1986.

187. J.T. Coyle, M.L. Oster-Granite and J.D. Gearhart. The neurobiologic consequences of Down Syndrome. Brain Res. Bull. 16:773-787, 1986.

188. J.D. Gearhart, H.S. Singer, T.H. Moran, M. Tiemeyer, M.L. Oster-Granite and

J.T. Coyle. Mouse chimeras composed of Trisomy 16 and normal (2N) cells: preliminary studies. Brain Res. Bull. 16:815-824, 1986.

189. P.J. Whitehouse, A.M. Martino, P.G. Antuono, P.R. Lowenstein, J.T. Coyle, D.L. Price and K.J. Kellar. Nicotinic acetylcholine binding sites in Alzheimer's Disease. Brain Res. 371:146-151, 1986.

190. C.S. Grob and J.T. Coyle. Suspected adverse methylphenidate-imipramine interactions in children. J. Dev. Behav. Pediatr. 7:265-267, 1986.

191. R.D. Blakely, L. Ory-Lavollee, R.C. Thompson and J.T. Coyle. Synaptosomal transport of radiolabel from N-Acetyl-Aspartyl-[3H]Glutamate suggests a mechanism of inactivation of an excitatory neuropeptide. J. Neurochem. 47:1013-1019, 1986.

192. P.R. Lowenstein and J.T. Coyle. Rapid regulation of [3H]Hemicholinium-3 binding sites in the rat brain. Brain Res. 381:191-194, 1986.

193. A.W. Deckel, T.H. Moran, J.T.Coyle, P.R. Sanberg and R.G. Robinson. Anatomical predictors of behavioral recovery following fetal striatal transplants. Brain Res. 365:249-197. 1986.

194. R.G. Struble, J. Lehmann, S.J. Mitchell, M. McKinney, D.L. Price, J.T. Coyle and M.R. DeLong. Basal forebrain neurons provide major cholinergic innervation of primate neocortex. Neurosci. Lett. 66:215-220, 1986.

195. A.W. Clark, C.L. White III, H.J. Manz, I.M. Parhad, B.Curry, P.J. Whitehouse, J. Lehmann and J.T. Coyle. Primary degenerative dementia without Alzheimer pathology. Can. J. Neurol. Sci. 13:462-470, 1986.

196. M.B. Robinson, R.D. Blakely and J.T. Coyle. Quisqualate selectively inhibits a brain peptidase which cleaves N-acetyl-L-aspartyl-L-glutamate *in vitro*. Eur. J. Pharmacol. 130:345-347, 1986.

197. M.D. Bunsey, P.R. Sanberg and J.T. Coyle. Topography of locomotor behaviour in the chick. Bird Behaviour 6:93-96, 1986.

198. J.M.H. ffrench-Mullen, T.H. Murphy, J.T. Coyle and R.S. Fisher. Dicarboxylic amino acids block epileptiform activity in rat hippocampal slice. Epilepsia 27:678-686, 1986.

199. M.L. Batshaw, S.L. Hyman, E. D. Mellits, G.H. Thomas, R. DeMuro and J.T. Coyle. Behavioral and neurotransmitter changes in the urease-infused rat: a model of congenital hyperammonemia. Pediatr. Res. 20:1310-1315, 1986.

200. J. Ferkany and J.T. Coyle. Heterogeneity of sodium-dependent excitatory amino acid uptake mechanisms in rat brain. J. Neurosci. Res.16:491-503, 1986.

201. R. Zaczek, A. Markle, M. Balm and J.T. Coyle. A simple method for quantitative electroencephalographic assessment of drugs with convulsant and anticonvulsant properties. J. Neurosci. Methods 18:351-360, 1986.

202. R. Zaczek, S. Arlis, A. Markl, T. Murphy, H. Drucker and J.T. Coyle. Characteristics of chloride-dependent incorporation of glutamate into brain

membranes argue against a receptor binding site. Neuropharmacology 26:281-287, 1987.

203. R.D. Blakely, L. Ory-Lavollee, R. Grzanna, K.J. Koller and J.T. Coyle. Selective immunocytochemical staining of mitral cells in rat olfactory bulb with affinity purified antibodies against N-acetyl-aspartyl-glutamate. Brain Res.402:373-378, 1987.

204. L. Ory-Lavollee, R.D. Blakely and J.T. Coyle. Neurochemical and immunocytochemical studies on the distribution of N-Acetyl-Aspartylglutamate and N-Acetyl-Aspartate in rat spinal cord and some peripheral nervous tissues. J. Neurochem.48:895-899, 1987.

205. M.D. Saltarelli, P.R. Lowenstein and J.T. Coyle. Rapid *in vitro* modulation of [3H]Hemicholinium-3 binding sites in rat striatal slices. Eur. J. Pharmacol.135:35-40, 1987.

206. P.R. Lowenstein, P.A. Slesinger, H.S. Singer, L.C. Walker, M.F. Casanova, D.L. Price and J.T. Coyle. An autoradiographic study of the development of [3H]Hemicholinium-3 binding sites in human and baboon basal ganglia: a marker for the sodium dependent high affinity choline uptake system. Dev. Brain Res. 34:291-297, 1987.

207. P.R. Sanberg, M.A. Henault, T.H. Moran, P.G. Antuono and J.T. Coyle. The development of daytime rearing behavior in methylazoxymethanol-treated rats: methodological considerations. Behav. Brain Res. 25:97-100, 1987.

208. R.H. Reeves, N.K. Robakis, M.L. Oster-Granite, H.M. Wisniewski, J.T. Coyle and J.D. Gearhart. Genetic linkage in the mouse of genes involved in Down Syndrome and Alzheimer's Disease in man. Molecular Brain Research 2:215-221, 1987.

209. R. Zaczek, M. Balm, S. Arlis, H. Drucker and J.T. Coyle. Quisqualate sensitive, chloride dependent transport of glutamate into rat brain synaptosomes. J. Neurosci. Res. 18-425-431, 1987.

210. R.D. Blakely, L. Ory-Lavollee and J.T. Coyle. Specific alterations in the levels of N-Acetyl-Aspartyl-Glutamate in the nervous system of the dystrophic mouse. Neurosci. Lett.79:223-228, 1987.

211. D.J. Braitman and J.T. Coyle. Inhibition of [3H]kainic acid receptor binding by divalent cations correlates with ion affinity for the calcium channel. Neuropharmacology 26:1247-1251, 1987.

212. C.F. Hohmann, G.L. Wenk, P. Lowenstein, M.E. Brown and J.T. Coyle. Age-related recurrence of basal forebrain lesion-induced cholinergic deficits. Neurosci. Lett. 82:253-259, 1987.

213. G. Forloni, R. Grzanna, R.D. Blakely, and J.T. Coyle. Co-localization of N-Acetyl-Aspartyl-Glutamate in central cholinergic, noradrenergic and serotonergic neurons. Synapse 1:455-460, 1987.

214. M.B. Robinson, R.D. Blakely, R. Couto and J.T. Coyle. Hydrolysis of the brain

dipeptide N-Acetyl-L-Aspartyl-L-Glutamate: identification and characterization of a novel N-Acetylated-Alpha-linked Acidic dipeptidase activity from rat brain. J. Biol. Chem. 262:14498-14506, 1987.

215. J.D. Gearhart, M.L. Oster-Granite, R.H. Reeves and J.T. Coyle. Developmental consequences of autosomal aneuploidy in mammals. Dev. Genet. 8:249-265, 1987.

216. M.D. Saltarelli, G.L. Forloni, M.L. Oster-Granite, J.D. Gearhart and J.T. Coyle. Neurochemical characterization of embryonic brain development in Trisomy 19 (TS19) mice: implications of selective deficits observed for abnormal neural development in aneuploidy. Dev. Genet. 8:267-279, 1987.

217. P.T. Joshi, J.A. Capozzoli and J.T. Coyle. Low dosage neuroleptic therapy for childhood onset pervasive developmental disorder. Am. J. Psychiat.ry 145:335-338, 1988.

218. T.H. Murphy, A.T. Malouf, A. Sastre, R.L. Schnaar and J.T. Coyle. Calcium dependent glutamate cytotoxicity in a neuronal cell line. Brain Res. 444:325-332, 1988.

219. R.D. Blakely, M.B. Robinson, R.C. Thompson and J.T. Coyle. Hydrolysis of the brain dipeptide N-Acetyl-L-Aspartyl-L-Glutamate (NAAG): subcellular and regional distribution, ontogeny, and the effect of lesions on N-acetylated-alpha-linked acidic dipeptidase activity. J. Neurochem. 50:1200-1209, 1988.

220. M.L. Batshaw, S.L. Hyman, J.T. Coyle, M.B. Robinson, I.A. Qureshi, E.D. Mellits and S. Quaskey. Effect of sodium benzoate and sodium phenylacetate on brain serotonin turnover in the ornithine ranscarbamylase-deficient sparse-fur mouse. Pediatr. Res. 23:368-374, 1988.

221. P.A. Slesinger, P.R. Lowenstein, H.S. Singer, L.C. Walker, M.F. Casanova, D.L. Price and J.T. Coyle. The development of B_1 and B_2 adrenergic receptors in baboon brain: An autoradiographic study using [^{125}I]Iodocyanopindolol. J. Comp. Neurol. 273:318-329, 1988.

222. K. Yamada, M.D. Saltarelli, and J.T. Coyle. Solubilization and characterization of the [^{3}H]Hemicholinium-3 binding site in rat brain. J. Neurochem. 50:1759-1764, 1988.

223. C. Bendotti, G.L. Forloni, R.A. Morgan, M.L. Oster-Granite, R.H. Reeves, J.D. Gearhart and J.T. Coyle. Neuroanatomical localization and quantification of cerebrovascular amyloid peptide RNA following *in situ* hybridization in the brains of normal, aneuploid, and experimentally lesioned mice. Proc. Natl. Acad Sci. U.S.A. 85:3628-3632, 1988.

224. A.S. Guarda, M.B. Robinson, L. Ory-Lavollée, G.L. Forloni, R.D. Blakely and J.T. Coyle. Quantitation of N-Acetyl-Aspartyl-Glutamate in microdissected brain nuclei and peripheral tissues: findings with a novel liquid phase radioimmunoassay. Molecular Brain Research 3:223-232, 1988.

225. C.F. Hohmann and J.T. Coyle. Long-term effects of basal forebrain lesions on cholinergic, noradrenergic and serotonergic markers in mouse neocortex. Brain

Res. Bull. 21:13-20, 1988.

226. J.S. Sweeney, C.F. Hohmann, T.H. Moran and J.T. Coyle. A long-acting cholinesterase inhibitor reverses spatial memory deficits in mice. Pharmacol. Biochem. Behav. 31:141-147, 1988.

227. C.F. Hohmann, A.R. Brooks and J.T. Coyle. Neonatal lesions of the basal forebrain cholinergic neurons result in abnormal cortical development. Dev. Brain Res. 42:253-264, 1988.

228. R.D. Blakely, M.B. Robinson, A.S. Guarda and J.T. Coyle. A re-examination of the interaction of N-Acetyl-L-Aspartyl-L-Glutamate with a subpopulation of rat brain membrane L-[3H]Glutamate binding sites. Eur. J. Pharmacol. 151:419-426, 1988.

229. R.T. Robertson, C.F. Hohmann, J.L. Bruce and J.T. Coyle. Neonatal enucleations reduce specific activity of acetylcholinesterase but not choline acetyltransferase in developing rat visual cortex. Dev. Brain Res. 39:298-302, 1988.

230. K. Yamada, M.D. Saltarelli and J.T. Coyle. Involvement of Phospholipase A_2 in the regulation of [^{3}H]Hemicholinium-3 binding. Biochem. Pharmacol. 37:4367-4373, 1988.

231. M.D. Saltarelli, J. Lopez, P.R. Lowenstein and J.T. Coyle. The role of calcium in the regulation of [3H]Hemicholinium-3 binding sites in rat brain. Neuropharmacology 27:1301-1308, 1988.

232. T.H. Murphy, R.L. Schnaar, J.T. Coyle and A. Sastre. Glutamate cytotoxicity in a neuronal cell line is blocked by membrane depolarization. Brain Res. 460:155-160, 1988.

233. R. Kurlan, D. Goldblatt, R. Zaczek, K. Jeffries, C. Irvine, J.T. Coyle and I. Shoulson. Cerebrospinal fluid homovanillic acid and Parkinsonism in Huntington's Disease. Ann. Neurol. 24:282-284, 1988.

234. R. Kurlan, E. Caine, A. Rubin, C. Nemeroff, G. Bissette, R. Zaczek, J.T. Coyle, F.J. Spielman, C. Irvine, and I. Shoulson. Cerebrospinal fluid correlates of depression in Huntington's Disease. Arch. Neurol. 45:881-883, 1988.

235. C.F. Hohmann, R. Hamon, M.L. Batshaw and J.T. Coyle. Transient postnatal elevation of serotonin levels in mouse neocortex. Dev. Brain Res.43:163-166, 1988.

236. B.F. O'Hara, C. Bendotti, R.H. Reeves, M.L. Oster-Granite, J.T. Coyle and J.D. Gearhart. Genetic mapping and analysis of somatostatin expression in Snell dwarf mice. Mol. Brain Res. 4:283-292, 1988.

237. G. Tsai, G. Forloni, M.B. Robinson, B.L. Stauch and J.T. Coyle. Calcium-dependent evoked release of N-[3H]Acetylaspartylglutamate from the optic pathway. J. Neurochem. 51:1956-1959, 1988.

238. G. Forloni, K. Blake, C.H. Hohmann and J.T. Coyle. The postnatal expression of acetylcholinesterase in somatostatin-positive cells of mouse hippocampus.

Developmental Brain Research 48:73-85, 1989.

239. J.E. Sweeney, C.F. Hohmann, M.L. Oster-Granite and J.T. Coyle. Neurogenesis of the basal forebrain in euploid and trisomy 16 mice: an animal model for developmental disorders in Down Syndrome. Neuroscience 31:413-425, 1989.

240. B.L. Stauch, M.B. Robinson, G. Forloni, G. Tsai and J.T. Coyle. The effects of NAALADase inhibitors on [3H]NAAG catabolism *in vivo*. Neurosci. Lett. 100:295-300, 1989.

241. M. Miyamoto, S. Narumi, A. Nagaoka and J.T. Coyle. Effects of continuous infusion of cholinergic drugs on memory impairment in rats with basal forebrain lesions. J. Pharmacol. Exp. Ther. 248:825-835, 1989.

242. K. Yamada, M.D. Saltarelli and J.T. Coyle. Specificity of the activation of [^{3}H]Hemicholinium-3 binding by phospholipase A_2. J. Pharmacol. Exp. Ther. 249:836-842, 1989.

243. T.H. Murphy, M. Miyamoto, A. Sastre, R.L. Schnaar and J.T. Coyle. Glutamate toxicity in a neuronal cell line involves inhibition of cystine transport leading to oxidative stress. Neuron 2:1547-1558, 1989.

244. P.R. Lowenstein, P.A. Slesinger, H.S. Singer, L.C. Walker, M.F. Casanova, L.S. Raskin, D.L. Price and J.T. Coyle. Compartment specific changes in the density of choline and dopamine uptake sites and muscarinic and dopaminergic receptors during the development of the baboon striatum: a quantitative receptor autoradiographic study. J. Comp. Neurol. 288:428-446, 1989.

245. M. Miyamoto, T.H. Murphy, R.L. Schnaar and J.T. Coyle. Antioxidants protect against glutamate-induced cytotoxicity in a neuronal cell line. J. Pharmacol. Exp. Ther. 250:1132-1140, 1989.

246. J.E. Sweeney, P.S. Puttfarcken and J.T. Coyle. Galanthamine, an acetylcholinesterase inhibitor: a time course of the effects on performance and neurochemical parameters in mice. Pharmacol. Biochem. Behav. 34:129-137, 1989.

247. J.L. Meyerhoff, M.B. Robinson, M.A. Bixler, S.S. Richards and J.T. Coyle. Seizures decrease regional enzymatic hydrolysis of N-acetyl-aspartylglutamate in rat brain. Brain Res. 505:130-134, 1989.

248. W. Ma, C.F. Hohmann, J.T. Coyle and S. L. Juliano. Lesions of the basal forebrain alter stimulus-evoked metabolic activity in mouse somatosensory cortex. J. Comp. Neurol. 288:414-427, 1989.

249. M.D. Saltarelli, K. Yamada and J.T. Coyle. Phospholipase A_2 and [^{3}H]Hemicholinium-3 binding sites in rat brain: a potential second messenger role for fatty acids in the regulation of high-affinity choline uptake. J. Neurosci. 10:62-72, 1990.

250. M. Miyamoto and J.T. Coyle. Idebenone attenuates neuronal degeneration induced by intrastriatal injection of excitotoxins. Exp. Neurol. 108:38-45, 1990.

251. T.M. Murphy, R.L. Schnaar and J.T. Coyle. Immature cortical neurons are uniquely sensitive to glutamate toxicity by inhibition of cystine uptake. FASEB J. 4:1624-1633, 1990.

252. M.T. Caserta, P. Corsi, M.L. Oster-Granite and J.T. Coyle. Increased number of somatostatin-immunoreactive neurons in primary cultures of Trisomy 16 mouse neocortex. Molecular Brain Research 7:269-272, 1990.

253. C.G. Frondoza, S. Logan, G. Forloni and J.T. Coyle. Production and characterization of monoclonal antibodies to N-Acetyl-Aspartyl-Glutamate. J. Histochem. Cytochem. 38:493-502, 1990.

254. P.R. Lowenstein, J.N. Joyce, J.T. Coyle and J.F. Marshall. Striosomal organization of cholinergic and dopaminergic uptake sites and cholinergic M_1 receptors in the adult human striatum: a quantitative receptor autoradiographic study. Brain Res. 510:122-126, 1990.

255. G. Forloni, C. Hohmann and J.T. Coyle. Developmental expression of somatostatin in mouse brain. I. Immunocytochemical studies. Devlopmental Brain Research 53:6-25, 1990.

256. C. Bendotti, C. Hohmann, G. Forloni, R. Reeves, J.T. Coyle and M.L. Oster-Granite. Developmental expression of somatostatin in mouse brain. II. In situ hybridization. Developmental Brain Research 53:26-39, 1990.

257. J.D. Rothstein, Tsai, G., Kuncl, R.W., Clawson, L., Cornblath, D.R., Drachman, D.B., Pestronk, A., Stauch, B.L. and Coyle, J.T. Abnormal excitatory amino acid metabolism in amyotrophic lateral sclerosis. Ann. Neurol. 28:18-25, 1990.

258. G. Tsai, B.L. Stauch, J.J. Vornov, J.K. Deshpande and J.T. Coyle. Selective release of N-acetylaspartylglutamate from rat optic nerve terminals *in vivo*. Brain Res. 518:313-316, 1990.

259. J.E. Sweeney, E.S. Bachman and J.T. Coyle. The effects of different doses of galanthamine, a long-acting acetylcholinesterase inhibitor, on memory in mice. Psychopharmacology 102:191-200, 1990.

260. B.Stauch Slusher, M.B. Robinson, G.Tsai, M.L. Simmons, S.S. Richards and J.T. Coyle. Rat brain N-acetylated alpha-linked acidic dipeptidase activity: purification and immunologic characterization. Journal Biological Chemistry 265:21297-21301, 1990.

261. P. Corsi and J.T. Coyle. Nerve growth factor corrects developmental impairments of basal forebrain cholinergic neurons in the trisomy 16 mouse. Proc. Natl. Acad. Sci. USA 18:1793-1797, 1991.

262. T.H. Murphy, M.J. DeLong and J.T. Coyle. Enhanced NAD(P)H: Quinone reductase activity prevents glutamate toxicity produced by oxidative stress. J. Neurochem. 56:990-995, 1991.

263. J.J. Vornov and J.T. Coyle. Glutamate neurotoxicity and the inhibition of protein synthesis in the hippocampal slice. J. Neurochem. 56:996-1006, 1991.

264. K. Kato, P.S. Puttfarcken, W.E. Lyons and J.T. Coyle. The developmental time course and ionic dependence of kainate mediated toxicity in rat cerebellar granule cell cultures. J. Pharmacol. Exp. Ther. 256:402-411, 1991.

265. K. Yamada, M.D. Saltarelli and J.T. Coyle. Effects of calmodulin antagonists on sodium-dependent high-affinity choline uptake. Brain Res. 542:132-134, 1991.

266. G.T. Capone, C. Bendotti, M.L. Oster-Granite and J.T. Coyle. Developmental expression of the gene encoding growth-associated protein 43 (GAP-43) in the brains of normal and aneuploid mice. J. Neurosci. Res. 29:449-460, 1991.

267. K. Yamada, M.D. Saltarelli and J.T. Coyle. [3H]Hemicholinium-3 binding in rats with status epilepticus induced by lithium and pilocarpine. Eur. J. Pharmacol. 195:395-397, 1991.

268. C.F. Hohmann, L. Wilson and J.T. Coyle. Efferent and afferent connections of mouse sensory-motor cortex following cholinergic deafferentation at birth. Cerebral Cortex 1:158-172, 1991.

269. C.F. Hohmann, K.K. Kwiterovich, M.L. Oster-Granite and J.T. Coyle. Newborn basal forebrain lesions disrupt cortical cytodifferentiation as visualized by rapid golgi staining. Cerebral Cortex 1:143-157, 1991.

270. J.J. Vornov and J.T. Coyle. Enhancement of NMDA receptor-mediated neurotoxicity in the hippocampal slice by depolarization and ischemia. Brain Res. 555:99-106, 1991.

271. P.T. Joshi, J.A. Capozzoli and J.T. Coyle. Neuroleptic malignant syndrome: life-threatening complication of neuroleptic treatment in adolescents with affective disorder. Pediatrics 87:235-239, 1991.

272. J. Piven, G. Tsai, E. Nehme, J.T. Coyle, G.A. Chase, S.E. Folstein. Platelet serotonin, a possible marker for familial autism. J. Autism Dev. Disord. 21:51-59, 1991.

273. G. Tsai, B. Stauch-Slusher, L. Sim, J.C. Hedreen, J.D. Rothstein, R. Kuncl and J.T. Coyle. Reductions in acidic amino acids and N-acetylaspartylglutamate in amyotrophic lateral sclerosis CNS. Brain Res. 556:151-156, 1991.

274. M.L. Simmons, C.G. Frondoza and J.T. Coyle. Immunocytochemical localization of N-acetyl-aspartate with monoclonal antibodies. Neuroscience 45:37-45, 1991.

275. J.J. Vornov, R.C. Tasker and J.T. Coyle. Direct observation of the agonist-specific regional vulnerability to glutamate, NMDA, and kainate neurotoxicity in organotypic hippocampal cultures. Exp. Neurol. 114:11-22, 1991.

276. J.T. Coyle, T.H. Murphy, P.S. Puttfarcken, E.W. Lyons and J.J. Vornov. The non-excitatory mechanisms of glutamate induced neurotoxicity. Epilepsy Res. 10: 41-48, 1991.

277. J.L. Meyerhoff, R.E. Carter, D.L. Yourick, B.S. Slusher, J.T. Coyle. Activity of a NAAG-hydrolyzing enzyme in brain may affect seizure susceptibility in genetically epilepsy-prone rats. Epilepsy Res.16:163-172,1992.

278. B.S. Slusher, G. Tsai, G. Yoo, J.T. Coyle. Immunocytochemical localization of the N-acetyle-glutamate (NAAG) hydrolyzing enzyme N-acetylated α–linked acidic dipeptidase (NAALADase). J Comp. Neurol. 315:217-229 1992.

279. M.B. Robinson, N.J. Anegawa, E. Gorry, I.A. Qureshi, J.T. Coyle, I. Lucki, M.L. Batshaw. Brain serotonin2 and serotonin $_{1A}$ receptors are altered in the congenitally hyperammonemic sparse fur mouse. Journal of Neurochem. 58:1016-1022, 1992.

280. J.L. Meyerhoff, R.E. Carter, D.L. Yourick, B.S. Slusher, J.T. Coyle. Genetically epilepsy-prone rats have increased brain regional activity of an enzyme which liberates glutamate from N-acetyl-aspartyl-glutamate. Brain Res. 593:140-143, 1992.

281. R.C. Tasker, J.T. Coyle, J.J. Vornov. The regional vulnerability to hypoglycemia-induced neurotoxicity in organotypic hippocampal culture: protection by early tetrodotoxin or delayed MK-801. J. Neurosci. 12:4298-4308, 1992.

282. S.Y. Han, J.E. Sweeney, E.S. Bachman, E.J. Schweiger, G. Forloni, J.T. Coyle, B.M. Davis, M.M. Joullie. Chemical and pharmacological characterization of galanthamine, and acetylcholinesterase inhibitor, and its derivatives. a potential application in Alzheimer's Disease. Eur. J. Med. Chem. 27:673-687, 1992.

283. P.S. Puttfarcken, J.S. Handen, D.T. Montgomery, J.T. Coyle, L.L. Werling. N-Acetyl-Aspartyl-L-Glutamate (NAAG) modulation of N-Methyl-D-Aspartate (NMDA)-stimulated [^{3}H]Norepinephrine release from rat hippocampal slices. J. Pharmacol. Exp. Ther. 266:796-803, 1993.

284. P.S. Puttfarcken, R.L. Getz and J.T. Coyle. Kainic acid-induced lipid peroxidation: protection with butylated hydroxytoluene and U78517F in primary cultures of cerebellar granule cells. Brain Res. 624:223-232, 1993.

285. G. Tsai, B.S. Slusher, L. Sim and J.T. Coyle. Immunocytochemical distribution of N-acetylaspartylglutamate in the rat forebrain and glutamatergic pathways. J. Chem. Neuroanat. 6:277-292, 1993.

286. G. Tsai, L.C. Cork, B.S. Slusher, D. Price and J.T. Coyle. Abnormal acidic amino acids and N-acetylaspartylglutamate in hereditary canine motoneuron disease. Brain Res. 629: 305-309, 1993.

287. J.T. Coyle and P. Puttfarcken. Oxidative stress, glutamate, and neurodegenerative disorders. Science 262:689-695, 1993.

288. C.A. Kitt, C. Hohmann, J.T. Coyle and D.L. Price. Cholinergic innervation of mouse forebrain structures. J. Comp. Neurol. 341:117-129, 1994.

289. J. J. Vornov, R.C. Tasker, and J.T. Coyle. Delayed protection by MK-801 and tetrodotoxin in a rat organotypic hippocampal culture model of ischemia. Stroke 25:457-465, 1994.

290. E.S. Bachman, J. Berger-Sweeney, J.T. Coyle and C.F. Hohmann. Developmental regulation of adult cortical morphology and behavior: an animal model for mental retardation. Int. J. Dev. Neurosci. 12:239-153, 1994.

291. U.V. Berger, R.E. Carter and J.T. Coyle. The immunocytochemical localization of N-Acetylaspartyl Glutamate, its hyrolysing enzyme NAALADase, and the NMDAR-1 receptor at a vertebrate neuromuscular junction. Neurosci. 64:847-850, 1995.

292. G. Tsai, D.R. Gastfriend and J.T. Coyle. The glutamatergic basis of human alcoholism. Am. J. Psychiatry 152:332-340, 1995.

293. L. Baer, P. Cukor, M.A. Jenike, L. Leahy, J. O'Laughlen and J.T. Coyle. Pilot studies of telemedicine in psychiatric patients with obsessive compulsive disorder. Am. J. Psychiatry 152:1383-1385, 1995.

294. D.C. Goff, G.C. Tsai, D.S. Monoach and J.T. Coyle. A dose-finding trial of D-cycloserine added to neuroleptics for negative symptoms in schizophrenia. Am. J. Psychiatry 152:1213-1215, 1995.

295. P.J. Schwartz, U.V. Berger and J.T. Coyle. Mice transgenic for Cu Zn superoxide dismutase exhibit increased markers on biogenic amine function. J. Neurochem. 65:660-669, 1995.

296. G. Tsai, L.A. Passani, B.S. Slusher, R. Carter, J.E. Kleinman and J.T. Coyle. Abnormal excitatory neurotransmitter metabolism in schizophrenic brains. Arch. Gen. Psychiatry 52:829-836, 1995.

297. G. Goff, G. Tsai and J.T. Coyle. Tardive dyskinesia and substrates of energy metabolism in cerebrospinal fluid. Am. J. Psychiatry 152:1730-1736, 1995.

298. L. Baer, D. Jacobs, P. Cukor, J. O'Laughlen, J.T. Coyle and K. Magruder. Fully automated telephone screening survey for depression. JAMA 273:1943-1944, 1995.

299. U.V. Berger, R.E. Carter, M. McKee and J.T. Coyle. N-acetylated alpha-linked acidic dipeptidase is expressed by non-myelinating Schwann cells in the peripheral nervous system. J. Neurocytol. 24:99-109, 1995.

300. A.R. Guimaraes, P. Schwartz, M.R. Prakash, C.A. Carr, U.V. Berger, B.G. Jenkins, J.T. Coyle and R.G. Gonzlez. Quantitative *in vivo* ^{1}H chemical shift imaging of excitotoxicity in rat brain. Neuroscience 69:1095-1101, 1995.

301. C.E. Peyser, M. Folstein, G.A. Chase, S. Starkstein, J. Brandt, J.R. Cockrell, F. Bylsma, J.T. Coyle, P.R. McHugh and S.E. Folstein. Trial of d-α-Tocopherol in Huntington's Disease. Am. J. Psychiatry 152:1771-1775, 1995.

302. R.E. Carter, A.R. Feldman and J.T. Coyle. Prostate-specific membrane antigen is a hydrolase with substrate and pharmacologic characteristics of a neuropeptidase. Proc. Natl. Acad. Sci. U.S.A. 93:749-753, 1996.

303. N.G. Ranen, C.E. Peyser, J.T. Coyle, F.W. Bylsma, M. Sherr, L. Day, M.F. Folstein, J. Brandt, C.A. Ross and S.E. Folstein. A controlled trial of idebenone in Huntington's Disease. Movement Disorders 11:549-554, 1996.

304. N.A. Simonian, R.L. Getz, J.C. Leveque, C. Konradi and J.T. Coyle. Kainic acid induces apoptosis in neurons. Neurosci. 74:675-683, 1996.

305. M. Didier, S. Bursztajn, E. Adamec, L. Passani, R. Nixon, J.T. Coyle, J.Y. Wei and S.A. Berman. DNA strand breaks induced by sustained glutamate excitotoxicity in primary neuronal cultures. J. Neurosci. 16:2238-2250, 1996.

306. D.C. Goff, G.Tsai, D.S. Monach, J. Flood, D.G. Darby and J.T. Coyle. D-Cycloserine added to clozapine for patients with schizophrenia. Am. J. Psychiatry 153:1628-1630, 1996.

307. L.A. Passani, J.P.G. Vonsattel. R.E. Carter and J.T. Coyle. N-acetyl-aspartylglutamate, N-acetylaspartate and N-acetylated alpha-linked acidic dipeptidase in human brain and their alterations in Huntington's and Alzheimer's disease. Mol. Chem. Neuropathol. 31:97-118, 1997.

308. L.A. Passani, J.P.G. Vonsattel and J.T. Coyle. Distribution of N-acetylaspartylglutamate immunoreactivity in human brain and its alteration in neurodegenerative disease. Brain Res. 772:9-22, 1997.

309. L.R. Orlando, R. Luthi-Carter, D.G. Standaert, J.T. Coyle, J.B. Penney, Jr. and A.B. Young. N-acetylaspartylglutamate (NAAG) protects against rat striatal quinolinic acid lesions *in vivo*. Neurosci. Letts. 236:91-94, 1997.

310. G. Tsai, D. C. Goff, R. W. Chang, J. Flood and J.T. Coyle. Markers of glutamatergic neurotransmission and oxidative stress associated with tardive dyskinesia. Am. J. Psychiatry 155:1207-1213, 1998.

311. G. Tsai and J.T. Coyle. The role of glutamatergic neurotransmission in the pathophysiology of alcoholism. Annual Review of Medicine 49:173-184, 1998.

312. R.L. Carter, U.V. Berger, A.K. Barczak, M. Enna and J.T. Coyle. Isolation and expression of a rat brain cDNA encoding glutamate carboxypeptidase II. Proc. Natl. Acad. Sci. U.S.A. 95:3215-3220, 1998.

313. P.J. Schwartz and J.T. Coyle. Effects of Overexpression of the Cytoplasmic Copper-Zinc Superoxide Dismutase on the Survival of Neurons *In Vitro*. Synapse 29:206-212, 1998.

314. P.J. Schwartz, A. Reaume, R. Scott and J.T. Coyle. Effects of over and under-expression of Cu, Zn-superoxide dismutase on the toxicity of glutamate analogs in transgenic mouse striatum, Brain Res. 789:23-39, 1998.

315. L. Passani, S. Elkabes and J.T. Coyle. Evidence for the presence of N-acetylaspartylglutamate in cultured oligodendrocytes and LPS activated microglia, Brain Research 794:143-145, 1998.

316. R. Luthi-Carter, A.K. Barczak, H. Speno and J.T. Coyle. Molecular characterization of human brain N-acetylated alpha-linked acidic dipeptidase (NAALADase). J. Pharmacol. Exp. Ther. 286:1020-1025, 1998.

317. R. Luthi-Carter, A.K. Barczak, H. Speno and J.T. Coyle. Hydrolysis of the neuropeptide N-acetylaspartylglutamate (NAAG) by cloned human glutamate carboxypeptidase II. Brain Res. 795: 1-2, 341-348, 1998.

318. G.E. Tsai, P. Ragan, R. Chang, S. Chen, V.M.I. Linnoila and J.T. Coyle. Increased glutamatergic neurotransmission and oxidative stress after alcohol withdrawal. Am. J. Psychiatry 155:6, 726-732, 1998.

319. C.H. Halsted, E. Ling, R. Luthi-Carter, J.A. Villanueva, J.M. Gardner and J.T. Coyle. Folypoly-γ-glutamate carboxypeptidase from pig jejunum: molecular characterization and relation to glutamate carboxypeptidase II. J. Biol. Chem. 273:20417-20424, 1998.

320. R. Bergeron, T.M. Meyer, J.T. Coyle and R.W. Greene. Modulation of NMDA receptor function by glycine transport. Proc. Natl. Acad. Sci. U.S.A. 95:15730-15734, 1998.

321. P. Crosi, G. Forloni, M. Troia, T. Lettini and J.T. Coyle. Somatostatin expression in TS16 mouse brain cultures. J. Mol. Neurosci. 10:99-111, 1998.

322. G. Tsai, D.P. van Kammen, S. Chen, M.E. Kelley, A. Grier and J.T. Coyle. Glutamatergic neurotransmission involves structural and clinical deficits of schizophrenia. Biol. Psychiatry 44:667-674, 1998.

323. G. Tsai, P. Yang, L.-C. Chung, N. Lange and J.T. Coyle. D-Serine added to antipsychotics for the treatment of schizophrenia. Biol. Psychiatry 44:1081-1089, 1998

324. H.S. Speno, W.L. Macias, R. Luthi-Carter, A.R.T. Joshi and J.T. Coyle. Site-directed mutagenesis of predicted active site residues in glutamate carboxypeptidase II. Mol. Pharmacol. 55:179–185, 1999 .

325. U.V. Berger, R. Luthi-Carter and J.T. Coyle. Glutamate Carboxypeptidase II is expressed by astrocytes in the rat nervous system. J. Comp. Neurology 415:52-64, 1999.

326. G.E. Tsai, W.E. Falk, J. Gunther and J.T. Coyle. Improved cognition in Alzheimer's disease with short-term D-cycloserine treatment. Am. J. Psychiatry 156:467-469, 1999.

327 Leski, S.L. Valentine and J.T. Coyle. L-type voltage-gated calcium channels modulate kainic acid neurotoxicity in cerebellar granule cells. Brain Res. 828:27-40, 1999.

328. G.E. Tsai, P. Yang, L-C Chung, I-C Tsai, C-W Tsai and J.T. Coyle. D-Serine Added to Clozapine for the Treatment of Schizophrenia. Am. J. Psychiatry 156:11, 1999.

329. C.R. Lindley, M.D. and J.T. Coyle. Psychopharmacologist as Family Doctor: Complications in the Joint Treatment of a Husband and Wife. Harvard Review of Psychiatry 7:222-229, 1999.

330. B.H. Price, R.D. Adams and J.T. Coyle. Neurology and Psychiatry: Closing the the Great Divide. Neurology 54:8-14, 2000.

331. J.T. Coyle. Psychotropic drug use in very young children. JAMA 283:1059-1060, 2000.

332. J.T. Coyle and R. Schwarcz. Mind Glue: Implications of Glial Cell Biology for Psychiatry. Arch. Gen. Psychiatry 57:90-93, 2000.

333. M.L. Leski, S.L. Valentine and J.T. Coyle. Insulin-like growth factor type-I prevents the development of sensitivity to kainate neurotoxicity in cerebellar granule cells. J. Neurochem. 75:1548-1556, 2000.

334. J-C. Leveque, W. Macias, A. Rajadhyaksha, R.R. Carlson, A. Barczak, S. Kang, X.-M. Li, J.T. Coyle, R.L. Huganir, S. Heckers and C. Konradi. Intracellular modulation of NMDA receptor function by antipsychotic Drugs. J. Neurosci. 20:4011-4020, 2000.

335. D.C. Goff, G. Tsai, J. Levitt, E. Amico, D. Monach, D. Schoenfeld, D.L. Hayden, R. McCarley and J.T. Coyle. A Placebo-controlled trial of D-Cycloserine added to conventional neuroleptics in patients with schizophrenia. Arch. Gen. Psychiatry 56:21-27, 2000.

336. T.V. Nguyen, A.L. Brownell, Y.C. Iris Chen, E. Livini, J.T. Coyle, B.R. Rosen and Cavagna F.J. Detection of the effects of dopamine receptor supersensitivity using pharmacologic correlations with PET. Synapse 36:57-65, 2000.

337. D. Goff and J.T. Coyle. The Emerging role of glutamate in the pathophysiology and treatment of schizophrenia. Am. J. Psychiatry 158:1367-1377, 2001.

338. J.T. Coyle and P. Kershaw. Galantamine, a cholinesterase inhibitor that allosterically modulates nicotinic receptors: effects on the course of Alzheimer's Disease. Biological Psychiatry 49:289-299, 2001.

339. J.T. Coyle. Drug treatment of anxiety disorders in children. N. Engl. J. Med. 344:1326-1327, 2001.

340. J.T. Coyle. Childhood mood disorders: Unmet needs but important opportunities. Biol. Psychiatry 49:959, 2001.

341. J.A. Frazier, R.Doyle, S. Chiu, J.T. Coyle. Treating a Child with Asperger's Disorder and Comorbid Bipolar Disorder. Am. J. Psychiatry 159:13-21, 2002.

342. M.L. Leski, L. Hassinger, S.L. Valentine, J.D. Baer and J.T. Coyle. L-Type calcium channels reduce ROS generation in cerebellar granule cells following kainate exposure. Synapse 43:30-41, 2002.

343. J.T. Coyle and H.K. Manji. Getting balance: drugs for bipolar disorder share target. Nature Medicine 8:557-558, 2002.

343. C. Flores and J.T. Coyle. Regulation of glutamate carboxypeptidase II function in corticolimbic regions of rat brain by phencyclidine, haloperidol, and clozapine. Neuropsychopharmacology 28:1227-1234, 2003.

345. J.T. Coyle and R.S. Duman. Finding the intracellular signaling pathways affected by mood disorder treatments. Neuron 38:157-160, 2003.

346. J.T. Coyle. Use it or Lose it: Do effort mental activities protect against dementia? New England Journal of Medicine 19:2489-2490, 2003.

346. J.T. Coyle, G. Tsai and D. Goff. Converging evidence of NMDA receptor hypofunction in the pathophysiology of schizophrenia. Ann. N.Y. Acad. Sci. 1003: 318-322, 2003.

346. G. Tsai, K.S. Dunham, U. Drager, A. Grier, C. Anderson, J. Collura and J.T. Coyle. Early embryonic death of glutamate carboxypeptidase II (NAALADase) homozygous mutants. Synapse 50:285-292, 2003.

346. J.T. Coyle, D.S. Pine, D.S. Charney, L. Lewis, C.B. Nemeroff, G.A. Carlson, P. Joshi, D. Reiss, R.D. Todd, M. Hellander, and the Depression and Bipolar support Alliance Consensus Development Panel. Depression and bipolar support alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in children and adolescents. J. Am. Acad. Child Adolesc. Psychiatry 42:1494-1503, 2003.

346. D.C. Javitt and J.T. Coyle. Decoding schizophrenia. Scientific American 290:38-45, 2004.

346. S. Ghose, C.S. Weickert, S.M. Colvin, J.T. Coyle, M.M. Herman, T.M. Hyde and J.E. Kleinman. Glutamate carboxypeptidase II gene expression in the human frontal and temporal lobe in schizophrenia. Neuropsychopharmacology 29:117-125, 2004.

346. J.T. Coyle and G. Tsai. The NMDA receptor glycine modulatory site: a therapeutic target for improving cognition and reducing negative symptoms in schizophrenia. Psychopharmacology, in press.

346. D.C. Goff, T. Bottiglieri, E. Arning, V. Shih, O. Freudenreich, A.E. Evins, D.C. Henderson, L. Baer, and J.T. Coyle. Folate, homocysteine, and negative symptoms in schizophrenia. Am. J. Psychiatry 161:179501708, 2004.

346. J.T. Coyle. The demise of old certitudes and the birth of novel opportunities in neuropsychopharmacology. Current Opinions in Pharmacology 4:1-3, 2004.

346. J.T. Coyle and G. Tsai. NMDA receptor function, neuroplasticity, and the pathophysiology of schizophrenia. International Review of Neurology 59:491-515, 2004.

346. D.A. Yurgelun-Todd, J.T. Coyle, S.a. Gruber, P.F. Renshaw, M.M. Silveri, E. Amico, B. Cohen and D.C. Goff. Functional magnetic resonance imaging studies of schizophrenic patients during word production: effects of D-cycloserine. Psychiatry Research Neuroimaging 138:23-31, 2004.

346. J.T. Coyle. The GABA-glutamate connection in schizophrenia: which is the proximate cause? Biochemical Pharmacology 68:1504-1514, 2004.

346. G. Tsai, R.J. Ralph-Williams, M. Martina, R. Bergeron, J. Berger-Sweeney, K.S. Dunham , Z. Jiang, S.B. Caine and J.T. Coyle. Gene knockout of the glycine transporter I: characterization of the behavioral phenotype. Proc. Natl. Acad. Sci. U.S.A.101:8485-8490, 2004.

346. M. Martina, M-E.B. Turcotte, S. Halman, G. Tsai, M. Tiberi, J.T. Coyle and R. Bergeron. Reduced glycine transporter type 1 expression leads to major changes

in glutamatergic neurotransmission of CA1 hippocampal neurones in mice. J. Physiol. 563:777-793, 2005.

346. M. Greene, K. Schill, S. Takahashi, A. Bateman-House, T. Beauchamp, H. Bok, D. Cheney, J. Coyle, T. Deacon, D. Dennett, P. Donovan, O. Flanagan, S. Goldman, H. Greely, L. Martin, E. Miller, A. Siegel, D. Solter, J. Gearhart, G. McKhann, R. Faden. Moral issues of human-non-human primate neural grafting. Science 309:385-386, 2005.

346. J.D. Picker and J.T. Coyle. Do maternal folate and homocysteine levels play a role in neurodevelopmental processes that increase risk for schizophrenia. Harvard Review of Psychiatry, in press.

346. J.T. Coyle. Glial metabolites of tryptophan and excitotoxicity: Coming unglued. Experimental Neurology, in press.

363. M.A. Frye, G.E. Tsai, T. Huggins, J.T. Coyle and R.M. Post. Low cerebrospinal fluid glutamate and glycine in refractory affective disorder. Biological Psychiatry, in Press.

Reviews and Chapters

1. S.H. Snyder, M.J. Kuhar, A.I. Green, J.T. Coyle and E.G. Shaskan. Uptake and subcellular localization of neurotransmitters in the brain. *Intern. Rev. Neurobiol.* 13:127-158, 1970.

2. S.H. Snyder, K.M. Taylor, A.S. Horn and J.T. Coyle. Psychoactive drugs and neurotransmitters: differentiating dopamine and norepinephrine neuronal functions with drugs. *Neuro. Res. Publ.* A.R.N.M.D. 50:359-375, 1972.

3. J.T. Coyle. Development of the central catecholaminergic neurons. *The Neurosciences: Third Study Program.* MIT Press (Cambridge), pp. 877-884, 1973.

4. J.T. Coyle. The development of catecholaminergic neurons of the central nervous system. In: ***Chemical Approaches to Brain Function, Neuroscience Research, Vol. 5***, Academic Press, New York, pp. 35-52, 1973.

5. J.T. Coyle. Development of the central catecholaminergic neurons of the rat. In: ***Frontiers in Catecholamine Research,*** (E. Usdin and S.H. Snyder, eds.), Pergamon Press, Inc., New York, pp. 261-267, 1973.

6. J.T. Coyle. Biochemical aspects of the catecholaminergic neurons in the brain of the fetal and neonatal rat. In: ***Dynamics of Degeneration and Growth in Neurons***, (K. Fuxe, L. Olson, and Y. Zutterman, eds.), Pergamon Press, Inc., New York, pp. 425-434, 1974.

7. J.T. Coyle. A practical introduction to radiometric enzymatic assays in psychopharmacology. In: ***Handbook of Psychopharmacology I*** (L.L. Iverson, S.D. Iversen and S.H. Snyder, eds.), Plenum Publishing Corp., New York, pp. 71-99, 1975.

8. J.T. Coyle. Neurochemical aspects of the development of the dopaminergic innervation to the striatum. In: ***Brain Dysfunction in Infantile***

Convulsions, (M.A.B. Brazier and F. Coceani, eds.), Raven Press, New York, pp. 25-39, 1976.

9. F. Garcin and J.T. Coyle. Ontogenetic development of [3H]-naloxone binding and endogenous morphine-like factors in rat brain. In: ***Cellular Effects of Opiates*** (H. Kosterlitz, ed.), North Holland Publ. Co., Amsterdam, pp. 267-273, 1976.

10. J.T. Coyle, R. Zaczek and P. Campochiaro. Changing relationships among neurotransmitter systems in developing striatum: implications for neuropsychopharmacology. Proc. 10th Collegium Internationale Neuro-Psychopharmacologicum, Pergamon Press, Oxford, 1363-1370, 1977.

11. J.T. Coyle. Biochemical aspects of neurotransmission in the developing brain. *Int. Rev. Neurobiol.* 20:65-103, 1977.

12. F. Garcin and J.T. Coyle. Ontogenetic development of [3H]-naloxone binding and endogenous morphine-like factor in rat brain. Proc. 10th Collegium Internationale Neuro-Psychopharmacologicum, Pergamon Press, 13:1379-1385, 1977.

13. J.T. Coyle. Discussion: Models in geriatric neuro-psychopharmacology. Proc. Collegium Internationale Neuro-Psychopharmacologicum, Pergamon Press, Oxford, 1179-1181, 1977.

14. J.T. Coyle. Psychiatric drugs in medical practice. In: ***Medical Clinics of North America*** (T. Reading and T.N. Wise, eds.), W.B. Sanders Co., Philadelphia, Vol. 61, pp. 891-905, 1977.

15. J.T. Coyle, P. Campochiaro and E.D. London. Neurotoxic action of kainic acid in the developing rat striatum. ***Maturation of Biochemical Neurotransmission Mechanisms***, Karger, Basil, pp. 134-141, 1977.

16. H.I. Yamamura, R.E. Hruska, R. Schwarcz and J.T. Coyle. Effect of striatal kainic acid lesions on muscarinic cholinergic receptor binding: correlation with Huntington's Disease. In: ***Animal Models in Psychiatry and Neurology*** (E. Usdin and I. Hanin, eds.), Pergamon Press, pp. 411-414, 1978.

17. S.R. Childers, R. Schwarcz, J.T. Coyle and S.H. Snyder. Radioimmunoassay of enkephalins: levels of methionine- and leucine-enkephalin in morphine-dependent and kainic acid-lesioned rat brain. In: ***The Endorphins, Vol. 18*** (E. Costa and M. Trabucchi, eds.), Raven Press, New York, 1978, pp. 161-173.

18. J.T. Coyle, K. Biziere and R. Schwarcz. Neurotoxicity of excitatory amino acids in the neural retina. In: ***Kainic Acid as a Tool in Neurobiology*** (P. McGeer, E. McGeer and J. Olney, eds.), Raven Press, New York, pp. 177-188, 1978.

19. R. Herndon and J.T. Coyle. Glutamatergic innervation, kainic acid, and vulnerability in the cerebellum. In: ***Kainic Acid as a Tool in Neurobiology*** (P. McGeer, E. McGeer and J. Olney, eds.), Raven Press, New York, 189-200, 1978.

20. J.T. Coyle. Neuronal mapping with kainic acid. *Trends Neurosci.* 132-135, 1978.

21. J.T. Coyle, K. Biziere, P. Campochiaro, R. Schwarcz and R. Zaczek. Kainic acid induced lesion of the striatum as an animal model for Huntington's Disease. In:

GABA Neurotransmitters, Alfred Benzon Symposium 12 (H. Kofod, P. Kroggsgaard-Larsen and J. Scheel-Kruger, eds.), Munksgaard, Copenhagen, pp. 419-431, 1978.

22. R. Schwarcz, K. Fuxe, Tomas Hokfelt, K. Andersson and J.T. Coyle. Dopamine and Huntington's disease: assessment using the kainic acid model. In: ***Dopaminergic Ergot Derivatives and Motor Function***, Pergamon Press, pp. 276-285, 1978.

23. J.T. Coyle, E.G. McGeer, P.L. McGeer and R. Schwarcz. Neostriatal injections: a model for Huntington's Chorea. In: ***Kainic Acid as a Tool in Neurobiology***. (E.G. McGeer, P.L. McGeer and J.W. Olney, eds.), Raven Press, New York. 139-159, 1978.

24. J.T. Coyle, K. Biziere, P. Campochiaro, E.D. London, R. Schwarcz and R. Zaczek. An animal model for Huntington's Disease: striatal kainic acid lesion. In: ***Catecholamines: Basic and Clinical Frontiers, Vol. 1***. (E. Usdin, I. Kopin and J. Barchas, eds.) pp. 751-756, 1979.

25. J.T. Coyle, M.V. Johnston and R. Grzanna. Development of the central noradrenergic neurons in the rat brain. In: ***Catecholamines: Basic and Clinical Frontiers, Vol. 1*** (E. Usdin, I. Kopin and J. Barchas, eds.) pp. 1608-1610, 1979.

26. J.T. Coyle. Pharmacotherapy of anxiety. *Psychiat. Ann.* 9:10-15, 1979.

27. J.T. Coyle, E.D. London, K. Biziere and R. Zaczek. Kainic acid neurotoxicity: Insights into the pathophysiology of Huntington's Disease. In: ***Advances in Neurology, Vol. 23*** (T.N. Chase, N.S. Wexler and A. Barbeau, eds.) Raven Press, New York, pp. 593-608, 1979.

28. J.T. Coyle. An animal model for Huntington's Disease: Striatal Kainic Acid Lesion. In: ***Etats Deficitairs Cerebraux Lies A L'Age, Symposium Bel-Air VI***, Evian, pp. 75-181, 1979.

29. J.T. Coyle. Excitatory Amino Acid Receptors. In: ***Neurotransmitter Receptors Part 1***. (S.J. Enna and H.I. Yamamura, eds.) Chapman & Hall, Ltd., London. pp. 5-40, 1980.

30. J.T. Coyle and J.B. Imboden. Management of psychiatric disorders. In: ***The Principles and Practice of Medicine, 20th Edition*** (A.M. Harvey, R.J. Johns, V.A. McKusick, A.H. Owens, R.S. Ross, eds.) Appleton-Century-Crofts, New York, pp. 1360-1369, 1980.

31. J.T. Coyle and M.V. Johnston. Neurochemical development of the brain. Proceedings of the 5th FDA Science Symposium, The Effects of Foods and Drugs on the Development and Function of the Nervous system: Methods for Predicting Toxicity. pp. 15-25, 1980.

32. J.R. DePaulo and J.T. Coyle. Haloperidol in Mania. In: ***Haloperidol Update: 1958-1980***. (F.J. Ayd, ed.) Waverly Press, Baltimore, pp. 66-72, 1980.

33. J.T. Coyle, R. Zaczek, J. Slevin and J. Collins. Neuronal receptor sites for kainic acid: correlations with neurotoxicity. In: ***Glutamate as a Neurotransmitter***

(G. DiChiara and G.L. Gessa, eds.) Raven Press, pp. 337-346, 1980.

34. J.T. Coyle. Striatal neuronal degeneration. Comparative Pathology Bulletin 7:3-4, 1980.

35. J.T. Coyle. Amino acid receptors: receptor binding techniques. Society for Neuroscience. 140-149, 1980.

36. J.T. Coyle and S.H. Snyder. Catecholamines. In: ***Basic Neurochemistry***, (G.J. Siegal, R.W. Albers, R. Katzman, B.W. Agranoff, eds.), Little Brown and Company, Boston, 205-217, 1981.

37. J.T. Coyle, J. Slevin, E.D. London, K. Biziere and J. Collins. Characterization of neuronal recognition sites for [3H]-kainic acid. In: ***Psychopharmacology and Biochemistry of Neurotransmitter Receptors***, (H.I. Yamamura, R.W. Olsen, E. Usdin, eds.), Raven Press, 501-514, 1981.

38. L. Tune, P. McHugh, and J.T. Coyle. Management of extrapyramidal side-effects induced by neuroleptics. Johns Hopkins Med. J. 148:149-153, 1981.

39. J.T. Coyle, M. McKinney and M.V. Johnston. Cholinergic innervation of the cerebral cortex: implications for the pathophysiology of senile dementia of the Alzheimer's type. In: ***Brain Neurotransmitters and Receptors in Aging and Age-Related Disorders*** (T. Samorajski, B. Beer and S.J. Enna, eds.) Raven Press, 149-161, 1981.

40. J.T. Coyle and M.V. Johnston. Ontogeny of the biochemical basis for neurotransmission: implications for neuropsychotropic drug action. In: ***Age and the Pharmacology of Psychoactive Drugs*** (Raskin, A., Robinson, D.S., and Levine, J., eds.) Elsevier North-Holland, Inc., Harvard, Mass., 47-62, 1981.

41. J.T. Coyle (Chairman), ***Excitatory Amino Acid Neurotoxins: Selectivity, Specificity, and Mechanism of Action. Neurosciences Research Program Bulletin***, 19, No. 4, 331-427, 1981.

42. M.V. Johnston and J.T. Coyle. Development of central neurotransmitter systems. ***The Fetus and Independent Life*** (Ciba Foundation), Pitman, London, pp. 251-270, 1981.

43. L. Tune, P. McHugh, and J.T. Coyle. Drug management in chronic schizophrenia. Johns Hopkins Med. J. 150:45-48, 1982.

44. M. McKinney, J. Hedreen and J.T. Coyle. Cortical cholinergic innervation: implications for the pathophysiology and treatment of senile dementia of the Alzheimer's type. In: ***Alzheimer's Disease: A Report of Progress.*** (S. Corkin et al, eds.) Raven Press, New York, pp. 259-265, 1982.

45. H.S. Singer, L.E. Tune, I.J. Butler, R. Zaczek and J.T. Coyle. Clinical symptomatology, CSF neurotransmitter metabolites and serum haloperidol levels in Gilles de la Tourette syndrome. In: ***Advances in Neurology, Vol. 35*** (A. Friedhoff and T. Chase, eds.), Raven Press, New York, pp. 177-183, 1982.

46. L.E. Tune and J.T. Coyle. Neuroleptic drug level monitoring in psychiatry: focus on radioreceptor assay techniques. Ther. Drug Monit. 4:59-64, 1982.

47. M.V. Johnston and J.T. Coyle. Cytotoxic lesions and the development of transmitter systems. Trends Neurosci. 5:153-156, 1982.

48. J.T. Coyle. Excitatory amino acid neurotoxins. In: ***Handbook of Psychopharmacology*** (L.L. Iversen, S.D. Iversen, S.H. Snyder, Eds.) Plenum, London, 237-269, 1982.

49. K. Biziere, J.T. Slevin, R. Zaczek, J.C. Collins, and J.T. Coyle. Kainic acid: neurotoxicity and receptor interactions. In: ***Advances in Pharmacology and Therapeutics II***, (H. Yoshida, Y. Hagihara and S. Ebashi, eds.) Vol. 1, 271-276, Pergamon Press, Oxford and New York, pp. 271-276, 1982.

50. D.L. Price, P.J. Whitehouse, R.G. Struble, J.T. Coyle, A.W. Clark, M.R. DeLong, L.C. Cork and J.C. Hedreen. Alzheimer's Disease and Down's Syndrome, Ann. N.Y. Acad. Sci. 396:145-164, 1982.

51. J.T. Coyle, The clinical use of antipsychotic medications. In: ***The Medical Clinics of North America***, Vol. 66 No.5:993-1009, 1982.

52. J.T. Coyle. Neurotoxic amino acids in human degenerative disorders. Trends in Neurosci. 5:287-288, 1982.

53. J.T. Coyle. Development of neurotransmitters in neocortex. In: ***Development and modifiability of the cerebral cortex***. (P. Rakic and P.S. Goldman-Rakic, eds.) Neurosci. Res. Prog. Bull. 20:479-491, 1982.

54. J.T. Coyle, D.L. Price, and M.R. DeLong. Brain mechanisms in Alzheimer's Disease. Hospital Practice pp. 55-63, 1982.

55. J.T. Coyle and R. Schwarcz. The use of excitatory amino acids as selective neurotoxins. In: ***Handbook of Chemical Neuroanatomy Vol.1: Methods in Chemical Neuroanatomy***. (A. Bjorklund and T. Hokfelt, eds.) Elsevier/North-Holland, 508-527, 1983.

56. S.J. Enna and J.T. Coyle. Neuroleptics. In: ***Neuroleptics: Neurochemical, Behavioral and Clinical Perspectives*** (J.T. Coyle and S.J. Enna, eds.) Raven Press, New York, 1-14, 1983.

57. G. Pearlson and J.T. Coyle. The dopamine hypothesis and schizophrenia. In: ***Neuroleptics: Neurochemical, Behavioral and Clinical Perspectives***, (J.T. Coyle and S.J. Enna, eds.) Raven Press, New York, 297-324, 1983.

58. J.T. Coyle and L.E. Tune. Radioreceptor assay for measurement of anticholinergic drugs in serum. In: ***Clinical Pharmacology in Psychiatry***. (L. Gram, E. Usdin, S.G. Dahl, P.Kragh-Sorensen, F. Sjoqvist and P.L. Morselli, eds.) The MacMillan Press, London and Basingstoke, pp. 150-164, 1983.

59. J.T. Coyle, M. McKinney, M.V. Johnston and J. Hedreen. Synaptic neurochemistry of the basal forebrain cholinergic projection of the rat. *Biological Aspects of Alzheimer's Disease*, Cold Spring Harbor, 223-241, 1983.

60. I. Hanin, J.T. Coyle, W.C. DeGroat, A. Fisher and C.R. Mantione. Chemically induced cholinotoxicity in vivo: studies utilizing ethylcholine aziridinium ion

(AF64A). *Biological Aspects of Alzheimer's Disease*, Cold Spring Harbor, pp.243-253, 1983.

61. J.T. Coyle, J. Ferkany, R. Zaczek, J. Slevin and K. Retz. Kainic acid: insights into its receptor-mediated neurotoxic mechanisms. In: ***Excitotoxins***. Wenner-Gren International Symposium Series, Vol. 9, (K. Fuxe, P. Roberts, R. Schwartz, eds.), Macmillan Press, London, pp. 112-121, 1983.

62. P.R. Sanberg and J.T. Coyle. Scientific approaches to Huntington's disease. CRC Critical Reviews in Clinical Neurobiology. Vol. 1, Issue 1, pp. 1-44, 1984.

63. J. Imboden and J.T. Coyle. Affective disorders. In: ***The Principles and Practice of Medicine, 21st Edition***, (Harvey, A.M., Johns, R.J., McKusick, V.A., Owens, A.H. and Ross, R.S., eds), Appleton-Century Crafts, Norwalk, pp. 1367-1372, 1984.

64. N. Paulker and J.T. Coyle. The schizophrenic disorders. In: ***The Principles and Practice of Medicine, 21st Edition***, (Harvey, A.M., Johns, R.J., McKusick, V.A., Owens, A.H. and Ross, R.S., eds.), Appleton-Century Crafts, Norwalk, pp. 1372-1379, 1984.

65. J. Imboden and J.T. Coyle. Neuroses and personality disorder. In: ***The Principles and Practice of Medicine, 21st Edition***, (Harvey, A.M. , Johns, R.J., McKusick, V.A., Owens, A.H. and Ross, R.S., eds), Appleton-Century Crafts, Norwalk, pp. 1385-1391, 1984.

66. J.T. Coyle, D. Price, M. DeLong. Anatomy of cholinergic projections to cerebral cortex: implications for the pathophysiology of senile dementia of the Alzheimer's type. Trends in Pharmacology, pp. 90-93., 1984.

67. P.R. Sanberg, D.A. Johnson, T.H. Moran and J.T. Coyle. Investigating locomotion abnormalities in animal models of extrapyramidal disorders: a commentary. Physiol. Psych. 12:48-50, 1984.

68. J.T. Coyle. Neuron-Specific Cytotoxins. In: ***Handbook of Neurochemistry***. (A. Lajtha, ed.) Plenum Publishing Co., New York, Vol. 9, pp. 299-329, 1985.

69. J.T. Coyle. Excitatory amino acid neurotoxins. In: ***IBRO Handbook Series - Methods in Neurosciences***, (G. Jaim-Etcheverry, ed.) pp. 123-41, 1985.

70. J.T. Coyle. Introduction to the pharmacology of the synapse. In: ***American Psychiatric Association Annual Review: Vol. IV***. (A.J. Francis, R.E. Hales, eds.), American Psychiatric Press, Inc., Washington, D.C., pp. 6-16, 1985.

71. J.T. Coyle. The Cholinergic Systems in psychiatry. In: ***American Psychiatric Association Annual Review: Vol. IV***. (A.J. Francis, R.E. Hales, eds.), American Psychiatric Press, Inc., Washington, D.C., pp. 49-66, 1985.

72. J.T. Coyle. Neurobiology of Alzheimer's Disease. In: ***Insights II. A Monograph of a Scientific Symposium of the National Mental Health Association***, Washington, D.C., pp. 11-15, October, 1985.

73. E.D. Bird and J.T. Coyle. Huntington's Disease. In: ***Clinical Neurochemistry, Vol. 1*** (H.S. Bachelar, G.G. Lunt and C.D. Marsden, eds.)

Academic Press Inc., London, pp. 1-57, 1986.

74. J.T. Coyle, J.D. Gearhart, M.L. Oster-Granite, H.S. Singer and T.H. Moran. Brain neurotransmitters: implications for Downs Syndrome from studies of mouse TS-16. In: ***The Neurobiology of Downs Syndrome*** (C. Epstein, ed.) New York, Raven Press, pp. 153-170, 1986.

75. J.T. Coyle. Aminergic projections from the reticular core. In: ***Diseases of the Nervous System, Vol II.*** (A. Asbury, G. McKhann and W. McDonald, eds.) Philadelphia, W.B. Saunders Company, pp. 880-889, 1986.

76. J.T. Coyle, R.D. Blakely, R. Zaczek, K.J. Koller, M. Abreu, L. Ory-Lavollee, R. Fisher, J.M.H. ffrench-Mullen and D.O. Carpenter. Acidic peptides in brain: do they act at putative glutamatergic synapses? In: ***Excitatory Amino Acids and Epilepsy*** (R. Schwarcz and Y. Ben-Ari, eds.) Plenum Press, New York, pp. 375-384, 1986.

77. J.T. Coyle and N. van Gelder. Commentary - Acidic excitatory amino acids and seizures: Neurochemical interrelationships. In: ***Excitatory Amino Acids and Epilepsy*** (R. Schwarcz and Y, Ben-Ari, eds.) Plenum Press, New York, pp. 385-387, 1986.

78. J.W. Ferkany and J.T. Coyle. Excitatory amino acid receptors. In: ***Neuromethods 4 - Receptor Binding*** (A.A. Goulton, G.B. Baker and P.D. Hrdina, eds.) Clifton, N.J., Humana Press, pp. 171-216, 1986.

79. J.T. Coyle. Clinical use of antipsychotic drugs. In: ***Clinical Psychopharmacology*** (L. Derogatis, ed.) Menlo Park, CA, Addison-Wesley Publishing Co., pp. 189-204, 1986.

80. R.S. Fisher, J.M.H. ffrench-Mullen, R. Zaczek, R. Blakely and J.T. Coyle. Dipeptides containing glutamate as endogenous neuroexcitatory agents. In: ***Neurotransmitters, Seizures and Epilepsy III*** (G. Nistico et al., eds.) Raven Press, New York, pp. 259-269, 1986.

81. R. Zaczek, K. Koller, D.O. Carpenter, R. Fisher, J.M.H. ffrench-Mullen and J.T. Coyle. Interactions of acidic peptides: excitatory amino acid receptors. In: ***Excitatory Amino Acid Transmitters*** (P.J. Roberts, H.S. Bradford and J. Storm-Mattisen, eds.), Macmillan, London, pp. 397-408, 1986.

82. R.G. Struble, J. Lehmann, S.J. Mitchell, L.C. Cork, J.T. Coyle, D.L. Price, M.R. DeLong and P.G. Antuono. Cortical cholinergic innervation: distribution, and source in monkeys. In: ***Dynamics of Cholinergic Function.*** (I. Hanin, ed.) New York, Plenum Press, pp. 23-30, 1986.

83. J.T. Coyle and J.C. Harris. The development of neurotransmitters and neuropeptides. In: ***Basic Handbook of Child Psychiatry.*** (J.D. Noshpitz, ed.) Basic Books, New York, pp. 14-25, 1987.

84. M.L. Batshaw, S.L. Hyman, C.Bachman, I.A. Qureshi and J.T. Coyle. Animal models of congenital hyperammonemia. In: ***Animal Models of Dementia: A Synaptic Neurochemical Perspective*** (J.T. Coyle, ed.), Alan R. Liss, Inc., New York, pp. 163-198, 1987.

85. P.R. Sanberg, T.H. Moran and J.T. Coyle. Microencephaly: cortical hypoplasia induced by methylazoxymethanol. In: ***Animal Models of Dementia: A Synaptic Neurochemical Perspective*** (J.T. Coyle, ed.), Alan R. Liss, Inc., New York, pp. 253-278, 1987.

86. M.L. Oster-Granite, J.D. Gearhart, R.H. Reeves, H.S. Singer, T.H. Moran and J.T. Coyle. Down Syndrome and the trisomy 16 mouse. In: ***Animal Models of Dementia: A Synaptic Neurochemical Perspective*** (J.T. Coyle, ed.), Alan R. Liss, Inc., New York, 1987, pp. 279-307, 1987.

87. J.T. Coyle. Kainic acid: insights into excitatory mechanisms causing selective neuronal degeneration. In: ***Selective Neuronal Death.*** (G. Bock and M.O'Conner, eds.) CIBA Foundation Symposium 126, John Wiley & Sons, Sussex, pp. 186-203, 1987.

88. J.T. Coyle. Alzheimer's disease. In: ***Encyclopedia of Neuroscience, Vol. I*** (G. Adelman, ed.) Birkhäuser, Boston, pp. 29-31, 1987.

89. J.T. Coyle. Excitotoxins. In: ***Encyclopedia of Neuroscience, Vol. I*** (G. Adelman, ed.) Birkhäuser, Boston, pp. 418-420, 1987.

90. J.T. Coyle. Excitotoxins. In: ***Psychopharmacology: The Third Generation of Progress.*** (H.Y. Meltzer, ed.) Raven Press, New York, pp. 333-340, 1987.

91. J.T. Coyle. Biochemical development of the brain: neurotransmitters and child psychiatry. In: ***Psychiatric Pharmacosciences of Children and Adolescents, Progress in Psychiatry*** (C. Popper, ed.), APA Press, 3-25, 1987.

92. M.B. Robinson and J.T. Coyle. Glutamate and related acidic excitatory neurotransmitters: from basic science to clinical application. FASEB J, 1:446-455, 1987.

93. M.L. Oster-Granite, J.T. Coyle, R.H. Reeves, H.S. Singer, T.H. Moran and J.D. Gearhart. Down Syndrome and the trisomy 16 mouse: relevance to Alzheimer's Disease. In: ***Molecular Neuropathology of Aging, Banbury Conference 27*** (Davies, P. and Finch, C., eds.) Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., pp. 387-398, 1988.

94. J.T. Coyle. Neuroscience and psychiatry. In: ***The American Psychiatric Press Textbook of Psychiatry.*** (J.A. Talbott, R.E. Hales and S.C. Yudofsky, eds.) American Psychiatric Press, Inc., Washington, pp. 3-32, 1988.

95. J.T. Coyle. Psychiatry, neuroscience, and the double disabilities. In: ***Mental Retardation and Mental Health: Classification, Diagnosis, Treatment, Services.*** (J. Stark, F. Menolascino, M. Albarelli and V. Grey, eds.) Springer-Verlag, New York, pp. 81-89, 1988.

96. C. Hohmann, P. Antuono and J.T. Coyle. Basal forebrain cholinergic neurons and Alzheimer's Disease. In: ***Handbook of Psychopharmacology, Vol. 20.*** (L.L. Iversen, S.D. Iversen and S.H. Snyder, eds.) Plenum Press, New York, pp. 69-106, 1988.

97. R.D. Blakely and J.T. Coyle. The neurobiology of N-Acetyl-Aspartyl Glutamate.

In: ***International Review of Neurobiology, Vol. 30*** (J.R. Smythies and R.J. Bradley, eds.) Academic Press, San Diego, pp.39-99, 1988.

98. J.T. Coyle, M.L. Oster-Granite, R.H. Reeves and J.D. Gearhart. Down syndrome, Alzheimer's disease and the trisomy 16 mouse. Trends Neurosci. 11:390-394, 1988.

99. M.L. Oster-Granite, R.H. Reeves, J.D. Gearhart and J.T. Coyle. Disorders of the developing nervous system of the trisomy 16 mouse: relevance to Down Syndrome and Alzheimer's Disease. In: ***Disorders of the Developing Nervous System: Changing Views of Their Origins, Diagnoses, and Treatments*** (Messer, A., ed.) Proc. Birth Def. Conf. XVIII, Alan R. Liss, Inc., New York, pp. 155-181, 1988.

100. J.T. Coyle and J.B. Imboden. Affective disorders and anxiety disorders In: ***The Principles and Practice of Medicine, 22nd Edition*** (A.M. Harvey, R.J. Johns, V.A. McKusick, A.H. Owens, R.S. Ross, eds.) Appleton & Lange, Conn., pp.1124-1130, 1988.

101. G. Pearlson and J.T. Coyle. Schizophrenia In: ***The Principles and Practice of Medicine, 22nd Edition*** (A.M. Harvey, R.J. Johns, V.A. McKusick, A.H. Owens, R.S. Ross, eds.) Appleton & Lange, Conn., pp. 1130-1135, 1988.

102. R.H. Reeves, R.A. Morgan, C. Bendotti, M.L. Oster-Granite, J.T. Coyle and J.D. Gearhart. The mouse as a model for studies of Alzheimer's Disease. In: ***The Molecular Biology of Alzheimer's Disease*** (C. Finch and P. Davies, eds.) Cold Spring Harbor Press, pp. 129-136, 1988.

103. J.M. Baraban and J.T. Coyle. Receptors, monoamines and amino acids. In: ***Comprehensive Textbook of Psychiatry, Fifth Edition.*** (H.I. Kaplan and B.J. Sadock, eds.) Williams and Wilkins, Baltimore, pp. 45-52, 1989.

104. J.T. Coyle. Alzheimer's disease: recent advances from molecular biologic studies. In: ***Neuroscience Year: Supplement 1 to the Encyclopedia of Neuroscience.*** (G. Adelman, ed.) Birkhauser Boston Inc., pp. 10-11, 1989.

105. J.T. Coyle, M.B. Robinson, R.D. Blakely and G.L. Forloni. The neurobiology of N-Acetyl-Aspartyl-Glutamate. In: ***Allosteric Modulation of Amino Acid Receptors: Therapeutic Implications.*** (E.A. Barnard and E. Costa, eds.), Raven Press, New York, pp. 319-333, 1989.

106. J.T. Coyle. Alzheimer's Disease In: ***Abnormal States of Brain and Mind: Readings from the Encyclopedia of Neuroscience*** (ed. Adelman, G.) Birkauser Boston, Inc., pp. 9-10, 1989.

107. T. Murphy, A. Parikh, R. Schnaar and J.T. Coyle. Arachidonic acid metabolism in glutamate neurotoxicity. Ann. N.Y. Acad. Sci., 559:474-477, 1989.

108. J.T. Coyle. Alzheimer's Disease: recent advances from molecular biologic studies. In: ***Biomedical Advances in Alzheimer's Disease,*** Monograph Series, Symposium of **141st Ann. Mtg. of the** Psychiatric Association (C.B. Nemeroff, Chair), Montreal, Canada, J. Clin. Psychiat. 7:17-22, 1989.

109. J.T. Coyle, M. Miyamoto, T.H. Murphy and R.L. Schnaar. Idebenone protects

against excitotoxin-induced neuronal degeneration. In: ***Fundamental and Clinical Assessment of Drugs on Cerebral Circulation and Metabolism in Vascular Dementia: Focus on Idebenone***. Proceedings of the International Association of Gerontology XIVth World Congress, Professional Postgraduate Services, Tokyo, Japan, pp. 9-17, 1989.

110. C.F. Hohmann, G. Capone, M.L. Oster-Granite and J.T. Coyle. Transplantation of brain tissue from murine trisomy 16 into euploid hosts: Effects of gene imbalance on brain development. In: ***Progress in Brain Research, Vol. 82*** (S.B. Dunnett and S.-J. Richards, eds.), Elsevier, Amsterdam, pp. 203-214, 1990.

111. J.T. Coyle. Introduction to child psychiatry. In: ***Foundations of Psychiatry***, (K. Davis, H. Klar and J.T. Coyle, eds.) W.B. Saunders, Philadelphia, pp 129-130, 1991.

112. B.H. Sohmer and J.T. Coyle. Childhood psychopathology: diagnosis and treatment. In: ***Foundations of Psychiatry*** (K. Davis, H. Klar and J.T. Coyle, eds.) W.B. Saunders, Philadelphia, pp 172-182, 1991.

113. J.T. Coyle. Molecular biological and neurobiologic contributions to our understanding of Alzheimer's Disease. In: ***The American Psychiatric Press Review of Psychiatry, Volume X*** (A. Tasman, ed.) American Psychiatric Press, Inc., Washington, D.C., pp 515-527, 1991.

114. J.T. Coyle. Foreword to Neuroscience, Section IV. In: ***The American Psychiatric Press Review of Psychiatry, Volume X*** (A. Tasman, ed.) American Psychiatric Press, Inc., Washington, D.C., pp 397-403, 1991.

115. J.J. Vomov and J.T. Coyle. Mechanisms of neurotransmitter receptor actions In: ***Neurotransmitters and Epilepsy: Frontiers of Clinical Neuroscience, Vol. 11*** (R.S. Fisher and J.T. Coyle, eds.) Wiley-Liss, Inc., New York, pp 17-31, 1991.

116. R.S. Fisher and J.T. Coyle. Preface: Neurotransmitters and Epilepsy In: ***Neurotransmitters and Epilepsy: Frontiers of Clinical Neuroscience, Vol. 11*** (R.S. Fisher and J.T. Coyle, eds.) Wiley-Liss, Inc., New York, pp 247-252, 1991.

117. J.T. Coyle, B. Stauch-Slusher, G. Tsai, J. Rothstein, J.L. Meyerhoff, M. Simmons and R.D. Blakely. N-Acetyl-aspartyl glutamate: recent developments. In: ***Excitatory Amino Acids, Fidia Symposium Series Vol. 5***, (eds. B.S. Meldrum, F. Moroni, R.P. Simon, J.H. Woods) Raven Press Ltd., New York, pp. 69-77, 1991.

118. M. McKinney and J.T. Coyle. The potential for muscarinic receptor subtype-specific pharmacotherapy for Alzheimer's Disease. Mayo Clin. Proc. 66:1225-1237, 1991.

119. J.L. Meyerhoff, M.B. Robinson, K.J. Koller, M.A. Bixler and J.T. Coyle. Kindling increases brain levels of NAAG; seizures reduce activity of a NAAG-hydrolyzing enzyme. In: ***Advances in the Neurobiology of Epilepsy,*** (Avenzini, ed.) Demos Press, 37:297-305, 1992.

120. J.L. Meyerhoff, R.E. Carter, D.L. Yourick, B.S. Slusher and J.T. Coyle. Activity

of a NAAG-hydrolyzing enzyme in brain may affect seizure susceptibility in genetically epilepsy-prone rats. In: ***Molecular Neurobiology of Epilepsy*** (J. Engel, Jr., C. Wasterlain, E.A. Cavalheiro, U. Heinemann and G. Avanzini, eds.) Elsevier Science Publishers B.V., Amsterdam, The Netherlands, pp. 163-172, 1992.

121. J.T. Coyle, M.L. Oster-Granite, R. Reeves, C. Hohmann, P. Corsi and J. Gearhart. Down syndrome and the trisomy 16 mouse: Impact of gene imbalance on brain development and aging. In: ***Genes, Brain and Behavior*** (P. McHugh and V. McKusick, eds.) Raven Press, New York, 85-99, 1992.

122. J.L. Meyerhoff, M.B. Robinson, J.J. Koller, M.A. Bixler and J.T. Coyle. Kindling increases brain levels of NAAG and seizures reduce activity of a NAAG-hydrolyzing enzyme, NAALADase. In: ***Neurotransmitters in Epilepsy.*** (G. Avanzini, J. Engel Jr., R. Fariello and U. Heinemann, eds.) Elsevier Science Publishers B.V., Amsterdam, The Netherlands, pp. 297-305, 1992.

123. J.J. Vornov, R.C. Tasker, J.T. Coyle. The differential neurotoxicity of endogenous and exogenous excitatory neurotransmitter receptor agonists. Natural and Synthetic Neurotoxins, Academic Press Limited, 187-224, 1993.

124. J.T. Coyle. Neuropharmacology, Editorial overview. Current Opinion in Neurology and Neurosurgery 6:581-582, 1993.

125. P.T. Joshi, J.T. Coyle and J.T. Walkup. Pharmacotherapy in children and adolescents. In ***Handbook of Adolescent Inpatient Psychiatric Treatment***, (H.S. Ghuman and R.M. Sarles eds.) Brunner/Mazel, New York, pp. 104-131, 1994.

126. J.T. Coyle. The neuroscience perspective and the changing role of the psychiatrist: the challenge for psychiatric educators. Academic Psychiatry 19:202-207, 1995.

127. G. Tsai and J.T. Coyle. N-Acetylaspartate in neuropsychiatric disorders. Progress in Neurobiology 46:531-540, 1995.

128. J.M. Baraban and J.T. Coyle. Monamine neurotransmitters. In: ***Comprehensive Textbook of Psycyhiatry/VI , Vol. I*** (H.I. Kaplan and B.J. Sadock eds.) Williams & Wilkins, Baltimore, pp. 25-41, 1995.

129. J.T. Coyle. Molecules and mind: a new home for molecular research in psychiatry. Molecular Psychiatry 1:5-6, 1996.

130. N.A. Simonian and J.T. Coyle. Oxidative stress in neurodegenerative diseases. Annu. Rev. Pharmacol. Toxicol. 36:83-106, 1996.

131. J.T. Coyle. The glutamatergic dysfunction hypothesis for schizophrenia. Harvard Review of Psychiatry 3:241-53, 1996.

132. L. Baer, P. Cukor and J. Coyle. Telepsychiatry: application of telemedicine to psychiatry. In: ***Telemedicine Theory and Practice*** (R.L. Bashshur, J.H.Sanders, G.W. Shannon eds.), Charles C. Thomas Publ. Ltd., Springfield, Illinois, pp 265-288 1996.

133. J.T. Coyle. Neuroscience and psychiatric treatment in the next century. In: ***Neuroscience, Neurology and Health,*** World Health Organization.

134. R.E. Carter and J.T. Coyle. Glutamate carboxypeptidase II. In: ***Handbook of Proteolytic Enzymes*** (A.J. Barratt, N. Rawlings and J.F. Woessner eds.). (Academic Press Limited, London, England, pp 1434-1437, 1997.

135. J.T. Coyle. The salience of neuroscience in the education of psychiatrists. In: ***Acute Care Psychiatry: Diagnosis and Treatment*** (L.I. Sederer and A.J. Rothschild eds.), Williams & Wilkins, Baltimore, Maryland, pp 469-480, 1997.

136. J.T. Coyle. The Nagging Question of the Function of N-acetylaspartylglutamate. Neurobiology of Disease 4:231-237, 1997.

137. J.T. Coyle and J. Mallet. Disease, transplantation and regeneration. Current Opinion in Neurobiology 7:663-665, 1997.

138. J.T. Coyle. Alzheimer's disease, molecular biology and the future of rational neuropsychotropic drug development. ***In: Int. Acad. Biomed. Drug. Res.*** Basel, Karger, 13:76-83, 1998.

139. F. Benes and J.T. Coyle. Déja vu all over again. Biological Psychiatry, 43:781-782, 1998.

140. J.T. Coyle. Toxic environments, neuronal plasticity, and delinquency. In: ***Advancing Research on Developmental Plasticity: Integrating the Behavioral Science and Neuroscience of Mental Health.*** (D.M. Hann, L.C. Huffman, I. Lederhendler and D. Meinecke, eds.) U.S. Government Printing Office, Washington, D.C., pp 105-112, 1998.

141. R.J. Steingard, C. Schmidt and J.T. Coyle. Basic neuroscience: critical issues for understanding psychiatric disorders. In: ***Adolescent Psychiatric and Behavioral Disorders.*** (S.B. Friedman, D.R. DeMaso, eds.) Hanley & Belfus, Inc. Philadelphia, PA, pp 205-215, 1998.

142. J.T. Coyle and S.E. Hyman. The Neuroscientific Foundations of Psychiatry. In: ***Textbook of Psychiatry*** 3rd ed. (R.E. Hales, S.C. Yudofsky and J.A. Talbott, eds.) The American Psychiatric Press, Washington, D.C., pp 3-33, 1998.

143. J.T. Coyle. Foreword In: ***Handbook of Developmental Neurotoxicology*** 2nd ed., (W.Slikker, Jr. and L. W. Chang eds.) Academic Press, San Diego, CA, 1998.

144. J.T. Coyle. Ice-nine and human prion disease. Harvard Rev. Psychiatry 6:331-333, 1999.

145. J.T. Coyle. The neuroscience revolution and psychiatry. In: ***Psychiatry in the New Millennium*** (S. Weissman, M. Sabshin and H. Eist, eds.), American Psychiatric Press, pp 7-23, 1999.

146. J.T. Coyle. Foreword In: ***Textbook of Geriatric Neuropsychiatry***, (C.E. Coffey and J.L. Cummings eds.) American Psychiatric Press, Washington, DC, 2000.

147. J.T. Coyle. Foreword In: ***Functional Neuroimaging in Child Psychiatry***, (M. Ernst, J.M. Rumsey eds.) Cambridge University Press, Cambridge, U.K., 2000.

148. J.T. Coyle. Amino Acid Neurotransmitters. In: ***The Corsini Enclycopedia of Psychology and Behavioral Science, Vol. 1.*** (W. E. Craighead and C.B. Nemeroff eds.) John Wiley & Sons, New York, NY, pp 83 – 86, 2000.

149. M. Williams, J.T. Coyle, S. Shaikh and M.W. Decker. Same Brain, New Decade: Challenges in CNS Drug Discover in Postgenomic, Proteomic Era. In: ***Annual Reports in Medicinal Chemistry , Vol. 36,*** (D.W. Robertson, ed.) Academic Press, San Diego, CA, pp 1-10, 2001.

150. J.T. Coyle, M.L. Leski and J.H. Morrison. The diverse roles of L-glutamic acid in brain signal transduction. In: ***Neuropsychopharmacology: The Fifth Generation of Progress***, Lippincott Williams & Wilkins, New York, NY, pp 71-90, 2002.

151. G. Tsai and J.T.Coyle. Glutamatergic mechanisms in schizophrenia. In Annual Review of Pharmacology and Toxicology, Vol. 42, Annual Reviews, Palo Alto, CA, pp 165-179, 2002.

152 J.T. Coyle, G. Tsai and D.C. Goff. Ionotropic glutamate receptors as therapeutic targets in schizophrenia. Current Drug Targets, 1:183-189, 2002.

152. R.E. Carter and J.T. Coyle. 290. Glutamate carboxypeptidase II. In ***Handbook of Proteolytic Enzymes*** 2nd Edn. 960-963, 2004.

153. J.T. Coyle. The neurochemistry of schizophrenia. In: ***Basic Neurochemistry: Molecular, Cellular and Medical Aspects***, Elsevier, Inc., in press.

154. J.T. Coyle and J.B. Martin. For the optimal treatment of neuropsychiatric disorders: the rapprochement of neurology and psychiatry. In: ***The Convergence of Neuroscience, Behavioral Science, Neurology, and Psychiatry*** (M. Hager ed.) Josiah Macy, Jr. Foundation, New York, NY, pp 25 – 44. 2005.

Letters and Book Reviews

1. J.T. Coyle. Book Review: Psychotherapeutic Drugs. The Johns Hopkins Medical Journal 145:248, 1979.

2. J.C. Harris, L.E. Tune, M. Allen and J.T. Coyle. Management of akathisia in a severely retarded adolescent male with help of an anticholinergic drug assay. The Lancet II:414, 1981.

3. J.T. Coyle. Book Review: Glutamate Transmitter in the Central Nervous System. Trends Neurosci. 5:232, 1982.

4. J.T. Coyle. Senility and the Cholinergic Link. Executive Health Report, Vol. XIX (6), 1982.

5. J.W. Ferkany, R. Zaczek and J.T. Coyle. Matters Arising - Response to: the mechanism of kainic acid neurotoxicity. Nature 308:561, 1984.

6. F. Ayd, J.T. Coyle, L.E. Hollister and G.M. Simpson. Tardive dyskinesia and thioridazine (Letter to the Editor). Arch. Gen. Psychiatry 41:414-415, 1984.

7. J.T. Coyle and D. Henry. Citation classic: catecholamines in fetal and newborn rat

brain. Current Contents 27:18, 1984.

8. J.T. Coyle. Book Review: Dynamics of neurotransmitter function. (I. Hanin, ed.), J. Med. Chem. 27:1757-1758, 1984.

9. J.T. Coyle. Book Review: Neurotransmitter actions in the vertebrate nervous system. (M.A. Rogawski and J.L. Barker, eds.). Cell, 1986.

10. J.T. Coyle. Cost of brain disorders. Nature 358:184, 1992 (letter).

11. J.T. Coyle. Funding of NIMH Extramural Research. Science 264:1517, 1994, (letter).

12. J.T. Coyle. Is psychiatry dead? Harvard Medical Alumni Bulletin, 68:20-23, 1995.

13. J.T. Coyle. Food for thought. Nature Medicine 1:1006-1007, 1995.

14. P. Rakic and J.T. Coyle. We need more brain awareness. The Journal of NIH Research 9:14, 1997, (letter).

15. J.T. Coyle and R. Mollica. Commentary: Forum – Psychiatry in Medical Education: A core curriculum in psychiatry for medical students. (M.G. Gelder ed.), Current Opinions in Psychiatry 11:494-496,1998.

16. J.T. Coyle. Book Review. Brain policy: How the new neuroscience changes our lives and our politics. Nature 400:330, 1999.

17. J.T. Coyle. In Memoriam: Robert Dorwart Harvard Review of Psychiatry 8:211-212, 2000.

18. J.T. Coyle. A continuing commitment to excellence. Archives of General Psychiatry 59:977, 2002.

19. C.A. Tamminga and J.T. Coyle. Current Drug Targets CNS and Neurological Disorders, Schizophrenia, Preface, 1:2002.

EXHIBIT B

REVISED EXHIBIT B FOR OPENING EXPERT REPORT OF DR. JOSEPH T. COYLE

Documents

1. '318 Patent [JAN RAZ-0000001 - JAN RAZ-0000003]
2. Prosecution History of the '318 Patent as presented by the PTO [JAN RAZ-0000004 - JAN RAZ-0000256]
3. Paragraph IV Notice Filed by Alphapharm [JAN RAZ-0001032 - JAN RAZ-0001060]
4. Paragraph IV Notice Filed by Barr [JAN RAZ-0001061 - JAN RAZ-0001080]
5. Paragraph IV Notice Filed by Dr. Reddy's [JAN RAZ-0001002 - JAN RAZ-0001031]
6. Paragraph IV Notice Filed by Mylan [JAN RAZ-0000955 - JAN RAZ-0000976]
7. Paragraph IV Notice Filed by Par [JAN RAZ-0001081 - JAN RAZ 0001106]
8. Paragraph IV Notice Filed by Purepac [JAN RAZ-0000977 - JAN RAZ-0001001]
9. Paragraph IV Notice Filed by Teva [JAN RAZ-0000937 - JAN RAZ-0000954]
10. Johnson & Johnson Pharmaceutical Research & Development Medical Report, *Justification for Claim that Galantamine Functions as an Allosteric Potentiating Ligand (APL) on Nicotinic Receptors* [JAN RAZ 0188028- JAN RAZ188042]

Publications

1. Albuquerque EX, Pereira EFR. Alkondon M. Eisenberg HM, Maelicke A Neuronal nicotinic receptors and synaptic transmission in the mammalian central nervous system. In: Handbook of Experimental Pharmacology, VOL 1M: Neuronal nicotinic receptors, as: Clementi F, Fornasari D, Golli C, Springer Berlin, pp 337-358, 2000.

2. Albuquerque EX. Alkondon M, Pereira EF, Castro N, Schrattenholz A., Barbosa C. Bonfante-Cabarcas R., Aracava Y, Eisenberg H, Maelicke A. Properties of neuronal nicotinic acetylcholine receptors, pharmacological characterization and madutation of synaptic function. J Pharmacol Em Therap. 280: 1117-1136, 1996.

3. Alkondon M, Braga MFM, Periera EFR, Maelicke A, Albuquerque EX. α7 Nicotinic acetylcholine receptors and modulation of gabaergic synaptic transmission in the hippocampus. Eur J Pharmacol 393: 59-67, 2000.

4. Alkondon M, Pereira EFR, Eisenberg HM, Albuquerque EX. Choline and selective antagonists identify two subtypes of nicotinic acetylcholine receptors that modulate GABA release from CAI interneurons in rat hippocampal slices. J Neurosci 19: 2693-2705, 1999.

5. Alkondon M. Pereira EFR. Cortes WS, Maelicke A, Albuquerque. EX Choline is a selective agonist of α7 nicotinic acetylcholine receptors. Eur. J. Neurosci. 9: 2734-2742, 1997.

6. Ancoli-Israel, S., et al. Effects of Galantamine Versus Donepezil on Sleep in Patients With Mild to Moderate Alzheimer Disease and Their Caregivers: A Double-Blind, Head-to-Head, Randomized Pilot Study. Alzheimer Dis Assoc Disord Vol. 19, No. 4: pp. 240-245, October-December 2005.

7. Bartus et al. Cholinergic Hypothesis: Its History and Future. in Annals of the New York Academy of Science, 332-358 (Ohon, Gamzu and Corking 1985).

8. Becker et al., "The second generation of cholinesterase inhibitors: clinical and pharmacological effects," in R. Becker and E. Giacobini, "Cholinergic Basis for Alzheimer Therapy," 263-296 (Birkhauser 1991)

9. Bergamini Vand Baggiore P, La lussazione congenita dell'anca, problema di importanza sociale. Neurology Minerva Medice p. 3553-3558,1960.

10. Bickel U, Thomsen T, Fischer JP, Weber W. Kewitz H. Galantmine: phamacokinetics, tissue distribution and cholinesterase inhibition in brain of mice. Neuropharmacoiogy 30: 447-454, 1991.

11. Bores GM, Huger FP, Petko W et al. Pharmacologic evaluation of novei AlzheimePs disease therapeutics: acetylcholinesterase inhibitors related to galantamine. JPET 277: 728-738, 1996.

12. Christie, J. et al. Physostigmine and Arecoline: Effects of Intravenous Infusions in Alzheimer Presenile Dementia. British Journal of Psychiatry 138:46-50, Jan. 1981.

13. Darreh-Shori T: Abstract 15A. Sixth International Stockholm/Springfleid Symposium on Advances in Alzheimer Therapy. Stockholm, Sweden (2000)

14. Doods et al..Therapeutic Potential of CNS-Active M2Antagonists: Novel Structures and Pharmacology. Life Sciences 52:497-503, 1993.

15. Geerts, H. et al., "Brain Levels and Acetylcholinesterase inhibition With Galantamine and Donepezil in Rats, Mice, and Rabbits," in Brain Research 1033: 186-193, 2005.

16. Harbaugh, R., Intracerebroventricular Bethanechol Chloride Infusion in Alzheimer's Disease: Results of a Collaborative Double-Blind Study. Journal of Neurosurgery 71(4):481-6, Oct. 1989.

17. Kaufer D, Friedman A., Seidrnan S., Soreq H. Acute stress facilitates long-lasting changes in cholinergic gene expression. Nature 393: 373-377, 1998.

18. Kihara T, Shimohama S, Urushitaml M, Sawada H, Kimura J, Kume T, Maeda T. Abide A. Stimulation of $\alpha 4\beta 2$ nicotinic receptors inhibits β-amyloid toxicity. Brain Res. 792: 331-334, 1998.

19. Kosasa T, Kuriya Y, Matsui K, Yamanishi Y. Inhibitory effect of orally administered donepezil hydrochloride (E2020). a novel treatment lor Alzheimer's disease, on cholinesterase activity in rats. Eur J Pharmacol 389: 173-179, 2000.

20. Kostowski W. and Gumulka W. Note On The Ganglionic and Central Actions of Galantamine. *Int. J Neuropharmacol* 7: 7-14, 1968.

21. Krause RM, Buisson B., Bertrand S, Corringer PJ., Galzi JL., Changeux JP, Bemand D. Ivermectin: A positive allosteric effector of the α7 neuronal nicotinic acetylcholine receptor. Mol Pharmacol 53: 283-294, 1998.

22. Maelicke A, Albuquerque EX New approach to drug therapy in Alzheimer's dementia. Drug Disc Today 1: 53-59, 1996.

23. Maelicke A, Albuquerque EX. Allosteric modulation of nicotinic acetylcholine receptors as a treatment strategy for Alzheimer's disease. Eur J Pharmacol 393: 165-170, 2000.

24. Maelicke A, Samcchocki M, Albuquerque EX. Jostok A, Zerlin M. Allosteric sensitization of human nicotinic receptors by galantamine, a new treatment strategy for Alzheimer's disease. JNS 187: S56, 2001.

25. Maelicke A, Schrattenholz A, Albuquerque EX. Neuronal nicotinic acetylcholine receptors in non-neuronal cells, expression and renaturation of ligand binding domain and modulatory control by aitostencally acting ligands. In: Handbookof Pharmacology (eds. Clamenti F, Fornasari D, Coni C). Springer Berlin, vol 144: 477-496 , 2000.

26. Maelicke A, Schrattenholz A, Schröder H. Modulatory control by non-competitive agonists of nicotinic cholinergic neurotransmission in the central nervous system. Seminars Neurosci 7: 103-114, 1995.

27. Maelicke A. Allosteric modulation of nicotinic receptors as a treatment strategy for Alzheimer's disease, Dement Geriatr Cog Disord 11: 71-18, 2000.

28. Maelike A, Schrattenholz A, Samochocki M, Radina M. Albuquerque EX. Allosterically potentiating ligands of nicotinic receptors as a treatment strategy for Alzheimer's disease. Behav Brain Res. 113: 199-206, 2000.

29. Marks MJ. Pauly JR, Gross SD, Deneris ES, Hermans-Borgmeyer I, Heinemann SF. Collins. AC. Nicotine binding and nicotinic receptor subunit RNA after chronic nicotine treatment. J Neurosci. 12: 2765-2784, 1992.

30. Martin-Ruiz CM. Court JA, Molnar E, Lee M. Goni C. Mamalaki A, Tsouloufis T, Tzartos S, Ballard C, Perry RH., Perry EK. α4 but not α3 and α7 nicotinic acetylcholine receptor subunits are lost from the temporal cortex in Alzheimer's disease. J Neurochem 73: 1635-1640, 1999.

31. Newhouse PA, Potter A, Levin ED. Nicotinic system involvement in Alzheimer's and Parkinson's diseases. Implications for therapeutics. Drugs Aging 11: 206-228, 1997.

32. Newhouse PA. Potter A, Corwin J. Lenox R. Age-related effects of the nicotinic antagonist mecamylamine on cognition and behavior. Neuropsychophannacology 10: 93-107, 1994.

33. Newhouse PA. SunderiandT, Tariot PN. Blumhardt CL, Weingartner H. Mellow A., et al. Intravenous nicotine in Alzheimer's disease: a pilot study. Psychopharmacolagy 95: 171-1 75, 1988.

34. Nordberg A, Winblad B. Reduced number of (^{3}H) nicotine and (^{3}H) acetylcholine binding sites in the frontal cortex of Alzheimer brains. Neumsci Len 72: 115-119, 1986.

35. Nordberg A. Lundqvist A, Hartvig P. Kinetic analysis of regional (s)(-)"c-nicotine binding in normal and Aizheimer brains: in vivo assessment using positron emission tomography. Alzheimer Dis Assoc Disord 9: 21-27, 1895.

36. Nordberg A. Nilsoon-Haakansson L, Adem A. Hardy J. Alafuzoff I, Lai I. Herrera-Marschitz M. Winblad B. The role of nicotinic receptors in the pathophysiology of Alzheimer's disease. Pmg. Brain Res. 79: 353-362, 1989.

37. Peng X. Gemnich V, Anand R. Wang F, Lindstrom J. Chronic nicotine treatment up-regulates $\alpha 3$ AchRs and $\alpha 7$ AChRs expressed by the human neuroblastoma cell line SH-SY5Y. Mol. Pharmacol. 51: 778-784, 1997.

38. Pereira EFR, Alkondon M. Reinhardt S. Maelicke A, Peng X. Lindstrom J, Whiting P, Aibuquerque EX. Physostigmine and galanthamine: probes for a novel binding site on the $\alpha 4\beta 2$ subtype of neuronal nicotinic acetylcholine receptors stably expressed in fibroblast cells. J. Pharrnacol. Exp. mer, 270: 768-778, 1994.

39. Pereira EFR, Reinhardt-Maelicke S, Schrattenholz A. Maelicke A, Albuquerque EX. Identification and functional characterization of a new agonisf site on nicotinic acetylcholine receptors of cultured hippocampal neurons. J. Pharmacol. Exp. her. 265: 1474-1491, 1993.

40. Perry DC, Dávila-Garcia MI, Stockmeier CA, Kellar KJ. Increased nicotinic receptors in brains from smokers: membrane binding and autoradiography studies. J Pharmacol Exp Ther 289: 1545-1552, 1999.

41. Perry E, Morris C. Court J. Cheng A. Fairbairn A. McKeith I, Irving D, Brown A, Perry R. Alteration in nicotine binding sites in Parkinson's disease. Lewy Body Dementia and Alzheimer's disease, possible index of early neuropathology. Neuroscience 64: 385-395, 1995.

42. Potter A, Cowin J, Lang J. Piasecki M. Lenox R, Newhouse PA. Acute effects of the selective cholinergic channel activator (nicotinic agonist) ABT-418 in Alzheimer's disease. Psychopharmacology 142: 334-342, 1999.

43. Prozorovskii, V. B. Sensitization of Cholinergic Receptors of Striped Muscle To Acetylcholine. Byull. Eksp. Biol. Med. 67:56-59, 1969.

44. Revelli U and Grasso, E. Nivaline Therapy (Galanthus Nivalus) in Poliomyelitic Diseases, Minerva Medica, 58: 3242-3245, 1967.

45. Rinne JO. Sixth International Stockholm/Springfieild Symposium on Advances in Alzheimer Therapy, Stockholm, Sweden, p.130 (2000).

46. Rupniak, N., Comparison of the Effects of Selective and Nonselective Muscarinic Agonists on Cognition and Thermoregulation in Primates, *Journal of Neurological Sciences* 110(1-2):222-7, July 1992.

47. Sabbagh MN, Reid RT, Corey-Bloom J, Rao TS, Hansen LA, Alford M, Masliah E. Adem A. Lloyd GK. Thal W. Correlation of nicotinic binding with neurochemical markers in Alzheimer's disease. J. Neural. Transm 105: 709-717, 1998.

48. Sabey K, Paradiso K, Zhang J, Steinbach JH. Ligand binding and activation of rat nicotinic $\alpha 4\beta 2$ receptors stably expressed in HEK293 cells. J. Pharfnami. Exp. mer. 55: 58-66, 1999.

49. Santos MD, Alkondon M. Aracava Y, Eisenberg HM, Maelicke A, Albuquerque EX. Effects of pyridostigmine and galanthamine on synaptic transmission in the mammalian central nervous system. Soc Neurosci Abstr (in press) (2000).

50. Schrattenholz A, Godovac-Zimmermann J, Schafer HJ. Albuquerque EX, Maelicke A. Photoaffinity labeling of Torpedo acetylcholine receptor by physostigmine. Eur J Biochem 216: 671-677, 1993.

51. Schrattenholz A. Pereira EFR, Roth U, Weber KH, Albuquerque EX. Maelicke A. Agonist responses of neuronal nicotinic receptors are potentiated by a novel class of allosterically acting ligands. Mot. Pharmacol. 49: 1-6, 1996.

52. Schröder B. Reinhardt S. Schrattenholz A, McLane KE. Kretschmer A. Conti-Tronconi BM, Maeiicke A. Monoclonal antibodies FK1 and WF6 define two neighboring ligand binding sites on Torpedo acetylcholine receptor o-polypeptide. J Biol. Chem. 269: 10407-10416, 1994.

53. Schröder H, Giambini E, Struble RG, Zilles K. Maelicke A. Nicotinic cholinoreceptive neurons of the frontal cortex are reduced in Alzheimer's disease. Neurobiol. Aging 12: 269-262, 1991.

54. Soncrant, T. et al., Memory Improvement Without Toxicity During Chronic, Low Dose Intravenous Arecoline in Alzheimer's Disease, *Psychopharmacology* 112(4):421-7, 1993.

55. Stojanov EA. European Trends in Anesthesiology (O Mayerhofer, ed,) international Anesthesiology Clinics, Little, Brown & Co. Boston, Vol 3: 675-685, 1965.

56. Storch A. Schrattenholz A. Cooper JC. Abdel Ghani M, Gutbrod O. Weber K-H, Reinhardt S, Lobron C, Hemen B. SoskicV, Pereira EFR. Albuquerque EX, Menthfessel

C. Maelicke A. Physostigmine, galanthamine and codeine act as noncompetitive nicotinic agonists on clonal rat pheochromocytoma cells. Eur J Pharmacol. 290: 207-219, 1995.

57. Svenssson AL, Nordberg A. Tacrine interacts with an allosteric activator site on $\alpha 4\beta 2$ nAChRs in M10 cells. Neuroreport 7: 2201-2205, 1996.

58. Tariot et al. Multiple-Dose Arecoline Infusions in Alzheimer's Disease. Arch Gen Psychiatry, 45: 901-905, 1988.

59. Taylor P. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th edition (Hardman JG. Gilman AG. Limbird LE, eds.) McGraw-Hill. New York, p. 165 (1998).

60. Thal. Clinical Trials in Alzheimer Disease. in Katzman and Bick, Alzheimer Disease (1994)

61. Thompson, T. & Kewitz, H., Galanthamine Treatment in Senile Dementia of Alzheimer's Type: A Case Report, *in* Kewitz, H. *et al.*, eds., *Pharmacological Interventions on Central Cholinergic Mechanisms in Senile Dementia (Alzheimer's Disease)* 238-41 (W. Zuckschwerdt Verlag 1989)

62. Thomsen T, Kaden B, Fischer, JP, Bickel, U, Ban, Gusztony G, Cervos-Navarro J, Kewitz, H. Inhibition of acetylcholinesterase activity in human brain tissue and erythrocytes by galantamine, physostigmine and tacrine. Eur J Clin Chem Clin Biochem 29:487-492, 1991.

63. Tiseo PJ, Rogers SL, Friedhoff LT. Pharmacokinetic and pharmacodynamic profile of donepezil HCl following evening administration. Brit J Clin Pharm 46, Suppl 1:13-18, 1998.

64. Ueda M, Matsumura S., Kimoto S., Matsuda S.Studies on the Anticholinesterase and Twitch Potentiation Activities of Galantamine. Jap J Pharmacol. 12: 111-119, 1962.

65. Vincent GP. Pietrusiak N. Rumennik L. Sepinwall J. The effects of galanthamine, an acetylcholinesterase inhibitor, on learning and memory in mice and monkeys. Sac Neurosci Abstr 27.12, 1988.

66. Wang HY, Lee DSH. D'Andrea MR, Peterson PA, Shank RP, Reitz AB. β-Amyloid$_{1-42}$ bind to $\alpha 7$ nicotinic acetylcholine receptor with high affinity. J. Biol. Chem. 275: 5626-5632, 2000.

67. Warpman U. Nordberg A. Epibatidine and ABT 418 revsal selective losses of a4$\beta 2$ nicotinic receptors in Alzheimer brains. Neuroreport 6: 2419-2423, 1995.

68. Wenck, et al., Meamylamine Interactions with Galantamine and Donepezil: Effects on Learning, Acetylcholinesterase, and Nicotinic Acetylcholine Receptors. Neuroscience 117:439-447 (2003).

69. Whitehouse PJ. Hedreen JC. White CL III, Price DL Basal forebrain neurons in the dementia of Parkinson disease. Ann. Neurol 13: 243-248, 1983.

70. Whitehouse PJ. Martino AM, Antuono PG et al. Nicotinic acetylcholine binding sites in Alzheimer's disease. Brain Res. 1, 55-65, 1986.

71. Wilcox, et al. A Long-Term Comparison of Galantamine and Donepezil in the Treatment of Alzheimer's Disease. Drugs Aging 1003:20(10):777-789 (2003).

72. Wilson AL. Langley LK, Monley J, Bauer T, Rottunda S. McFalls E, Kovera C, McCarten JR. Nicotine patches in Alzheimer's disease: pilot study on learning, memory and safety. Pharmacol Biochem Behav 51: 509-514, 1995.

73. Wislicki L. Nivalin (Galanthamine Hydrobromide). An Additional Decurarizing Agent, Some Introductory Observations, Brit J. Anaesth. 39: 963-968, 1967.

74. Wonnawn S, Marks MJ. Nicotine: not just for cigarettes anymore. Drug Discovery Today 4(11): 490-492, 1998.

75. Wurtman, R.J., "Activation of neurotransmitters in the brain: strategies in the treatment of AD/SDAT" in C.G. Gottfries, Normal Aging, Alzheimer's Disease and Senile Dementia: Aspects on Etiology, Pathogenesis, Diagnosis and Treatment 275 -80, 1985.

76. Zwart R, Vijverberg HPM. Potentiation and inhibition of neuronal nicotinic receptors by atropine: competitive and noncompetitive effects. Md Pharmacol 52: 886-895, 1997.